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Informa Pharma Intelligence

Pharma R&D Annual Review

2021

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Introduction

Welcome to *Pharmaprojects'* 2021 review of trends in pharmaceutical R&D. For almost 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 2021. We'll assess industry trends by examining the pipeline by company, therapeutic area, disease, target and drug type, using data from Informa 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 entering the matrix databank, travelling through time back through 2020, and using our findings to project the course for pharma R&D as it navigates its way through one of the most turbulent periods of modern history, hopefully towards a new, gleaming, technologically advanced future.

Regular readers of this report (which has been running since 1993) will know that in recent years, I've threaded a different theme through each edition, to highlight points, to draw analogies, and to give a little turbo thrust into what could otherwise be a rather lengthy voyage through the subspace world of statistics, charts and tables. Themes selected so far have included astronomy, movies, the natural world, music and, last year, food and drink. After completing the 2020 report early last February, I thought science fiction might be a fun topic for 2021's report. Little did I know at that point that 2020 would turn out to resemble a particularly grim science fiction movie for all of us. A long time ago, in a galaxy far, far away – or last January as I prefer to call it – the world was a very different place indeed. Sure, there was this viral outbreak in China, but we'd been through these kinds of things before with SARS, MERS, swine flu, etc, right? Surely it would just fade away as before, and we and the pharma industry would continue our relentless march into the sunlit uplands of our golden futures.

Wrong. As SF author Frank Herbert wrote in his acclaimed *Dune* novel: *"Deep in the human unconscious is a pervasive need for a logical universe that makes sense. But the real universe is always one step beyond logic."* It's already become a cliché, but few people would have believed what they would see if they had been able to jump into a time machine last year and travel forward 12 months. Our hospitals under huge pressure, a mounting global death toll, economies devastated and our streets deserted. The latter has often led to citations of the 2002 British sci-fi film *28 Days Later*, where a man emerges from a coma to find London deserted following an outbreak of a rage-inducing virus. Another 'pandemic' science fiction movie, *Contagion*, from 2011, is probably closer to the mark, and reportedly received a huge spike in viewings during the year on streaming platform Netflix. Fears of alien invaders of all kinds are of course a staple of science fiction, dating from HG Wells' *The War of the Worlds*, published way back in 1898. Alien invasions have been covered throughout SF history, right through 1950s B-movie classics like *The Day the Earth Stood Still*, with its giant robot, Gort, and the chilling paranoia of *Invasion of the Body Snatchers*, up to more modern fare like the bombastic *Independence Day*. And different aliens seemed to be invading the same corner of Southeast England every few weeks in the 1970s in the long-running UK TV show *Doctor Who*.

So 2020 has been a bit like living inside a sci-fi movie, strange and fantastical, in all the wrong ways. However, if a year ago you'd told me about the pandemic, *and* told me that we'd already have six vaccines developed and being rolled out, less than a year since we made 'first contact' with the virus, then I really would have thought you had taken leave of your senses and entered a parallel universe. The global response, particularly from the pharmaceutical industry, has been nothing short of phenomenal. The previous record for developing a vaccine against a new pathogen was held by the Ebola virus vaccine, which took five years to develop. A decade is more commonplace. But instead of 10 years, we did this in 10 months. As a result, we can see a light at the end of the tunnel. The US government even borrowed a *Star Trek* term to help us to get here, calling its COVID-19 vaccine acceleration programme 'Operation Warp Speed'.

In the meantime, another effect of the pandemic, or rather measures introduced to attempt to control it, is the way it has made each of our worlds shrink. I was reminded of this recently while re-watching one of my favourite episodes of *Star Trek: The Next Generation*, 'Remember Me'. In the story, Dr Beverly Crusher's son Wesley's science experiment traps her in a bubble universe, unbeknownst to her. Gradually, people in her life seem to be disappearing or people don't seem to remember them. What is going on? It transpires that the bubble universe is contracting, and when her entire universe becomes smaller than the size of *The Enterprise*, it turns into a race against time to rescue the good doctor before the ship breaks up or the universe shrinks to nothing. (I won't spoil it by telling you what happens in the end, but you can probably guess.) This story seemed to me to have resonance for how our own personal universes shrank through 2020 as a result of COVID-19. A year ago, I was looking forward to a holiday in Thailand in February (which, fortunately, I was still able to enjoy), but since then international travel has all but disappeared, I've only left London once since March, and now I no longer even travel as far as into the office. As I write, the UK is in another strict lockdown and my universe has shrunk further to pretty much extend only as far as the walls of my apartment and the neighbourhood supermarket. Meanwhile, many friends have 'disappeared' from my personal universe, hopefully temporarily, and currently even close friends can only be glimpsed via the technological wonder of Zoom meetings. The effect of all this on people's mental health can be devastating, and, at times, you can feel like you're disappearing down your own personal wormhole. 'Is there anybody out there?' indeed.

One effect of this most science fiction-like of years has been to put the pharmaceutical industry centre stage like it never has been before. Who would have thought a year ago that we'd all become such experts on vaccine types, cytokine storms and R numbers? While the likes of Pfizer and AstraZeneca were probably household names beforehand, few outside of our own industry would have heard of BioNTech and Moderna a year ago. The pharma industry, which, let's face it, didn't have the greatest of public images, is now riding to all of our rescues. Whereas previously many viewed big pharma as some kind of nefarious shadowy enterprise, akin perhaps to the Tyrell Corporation in the 1982 SF masterpiece *Blade Runner*, now it is coming together to save the world more in the manner of *Avengers Assemble*. It is to be hoped that it can continue to build on its enhanced reputation in the months ahead as the vaccine challenge moves to be one which is more logistical than scientific. But we shouldn't underestimate the enormity of that challenge, for both pharma and governments. It's a sobering thought that tuberculosis, a disease for which there have been not only vaccines but drug treatments for decades, still manages to kill around 1.5 million people (just lower than the total number killed by COVID thus far) *every single year*. The challenge will not only be how to get vaccines to people in the developed world, but, as with TB, to get them to the world's poorest.

Aside from the fantastical nature of the events we're all living through, science fiction has always proved a useful tool for illuminating our lives. While much of the genre is speculative to the extreme, there has always been a place for SF to be used to reflect issues in today's world. The TV series *Black Mirror* has in recent years used the technique of seemingly taking us only a little into the future to highlight very real misgivings about technology and our social media use. Back in the 1960s, the original *Star Trek* series presented us, only 20 years after the end of the Second World War, with a hopeful future where alliances across a federation of planets and races had brought peace and understanding, while dealing more directly with contemporary issues in specific episodes like racism in *'Let That Be Your Last Battlefield'* or social inequality in *'The Cloud Minders'*. *Doctor Who's* nemeses the Daleks had clear allegorical comments on Nazism's obsession with racial purity. Going further back, George Orwell critiqued totalitarian regimes of the day in *Animal Farm* and *1984*. Sometimes, SF holds a lens up to help us to see ourselves better.

And let's not forget, science fiction is often great fun. I myself have been a lifelong fan, and it's entirely possible that it was the influence of SF TV as a child which led me to pursue a career in science fact. Being British, my number one was, and still is, *Doctor Who*, which has been running (with one notable hiatus) since 1963 (even slightly longer than I have). This eccentric and very British show may have had an alien flying around time and space in a police box fighting all manner of bizarre monsters and despots, but, crucially, the Doctor always wins the day by using logic, reason and science – not violence. This had a profound effect on me as a young boy.

So, in this report, I hope to use analogies from, and references to, science fiction books, films and TV shows to highlight and illuminate the changes which the pharmaceutical industry is going through, and what has changed for it over recent years. The effect of the COVID-19 pandemic has, as we shall see, made a significant impact in a very short space of time, so I'll be returning to it a lot. While I hope to keep the writing fun and lively, I do not wish to be flippant about the very real horror we are living through now, and appreciate that many readers will have been personally affected. For this reason, I want to dedicate this 18th edition of the Pharma R&D Annual Report to all those who have lost people to the pandemic, and all of you who are working tirelessly to help us get out of this situation, which I'm sure we will. If there's one thing a good sci-fi B-movie has taught us, it's the indomitable nature of humanity. Together, we'll see off this particular alien invader.

"I, for one, bet on science as helping us... Science has given us more lives than it has taken; we must remember that."

- Philip K Dick

Lift-Off: Total Pipeline Size

Pharma's universe continues to expand, despite 2020's dark matter

Let's engage our warp drive and jump straight into our analysis by looking at the overall size of the observable pharma universe: the total number of drugs currently in the pipeline. 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 stopped, or whose development is complete, are not included. All data were collected on January 4th, 2021.

A key question to answer this year is going to be what effect COVID-19 has had on pharma R&D as a whole. Many may have been left with the impression that the sudden stampede into all things corona-shaped has shifted resources away from other diseases, and slowed development, partly due to inevitable delays to clinical trials. This isn't always easy to tease out from the data, but a good place to start is to look at the total size of the pipeline now compared to that of a year ago. Should we be setting phasers to stun to reflect another big growth in the pipeline, or has the pandemic effectively put the industry into cryogenic sleep for the duration of the long voyage through 2020?

Well, Figure 1 does show a further increase in the overall pipeline size, but it is somewhat less than stratospheric. At 18,582 drugs, the pharma R&D pipeline has increased by 4.76% – still a reasonable rate of expansion, but only around half that seen in the previous 12 months, when it came in at 9.62%. But, for context, this sits roughly in the middle of the 2019 and 2018 figures of 5.99% and 2.66%, respectively, so it's by no means an outlier in terms of recent growth rates.

This means that there are 845 more drugs in development now than there were this time last year. But how much of this increase can be accounted for by new therapies and vaccines to treat or prevent COVID-19 itself? We'll be looking into that in more detail later, but we can report 798 new COVID-specific drugs or vaccines were added to the database during the year. Does this mean that the rest of pharma R&D went into stasis?

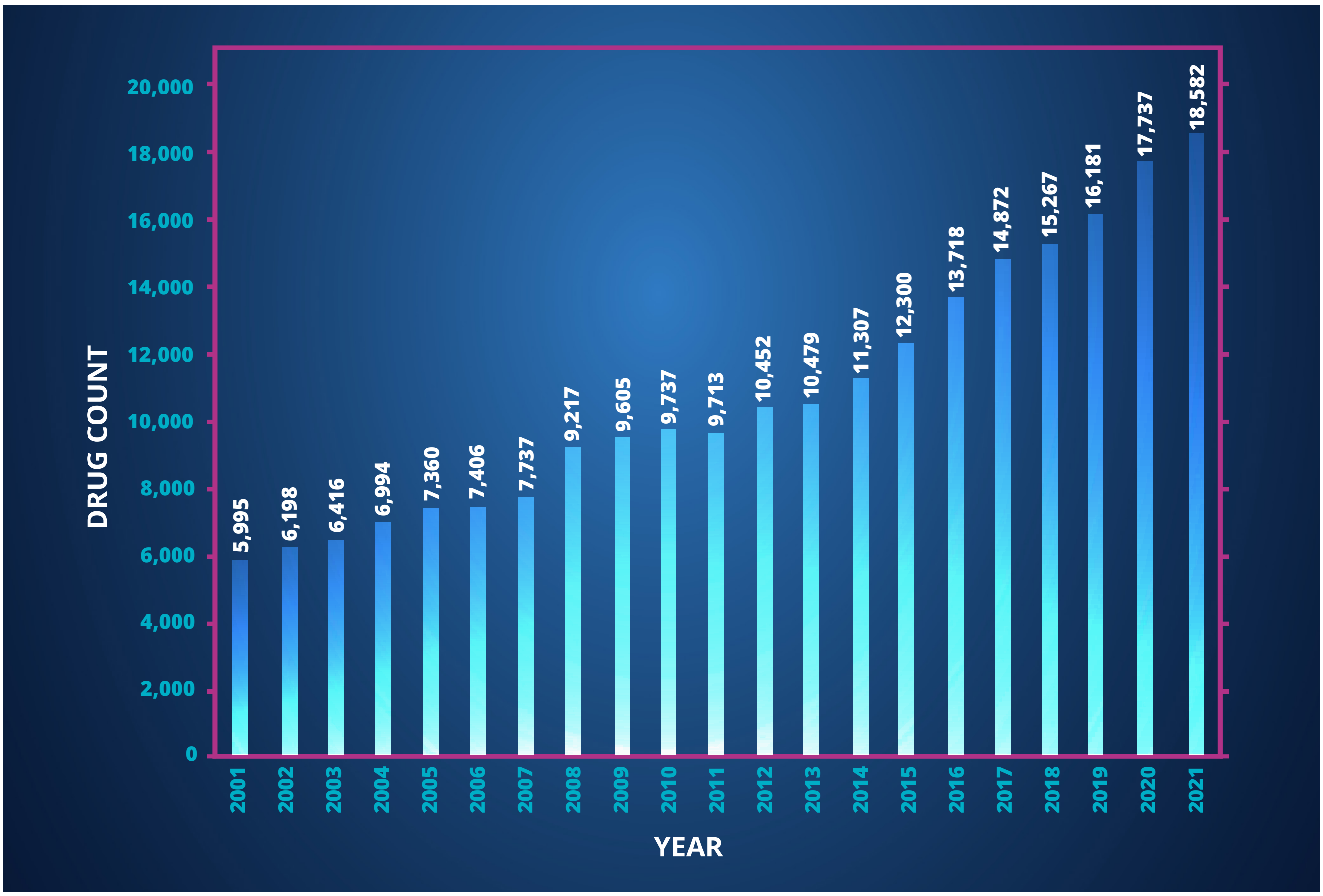
In fact, there were 5,544 new drugs added to the *Pharmaprojects* database during the year, which compares to 4,730 through 2019. So, by this metric, those new COVID drugs were just *extra*; the industry discovered almost exactly the same number of non-COVID drugs as in the pre-COVID days. No evidence here then of industry endeavour curtailed by the disease – the Force is still very much with it!

In fact, there is another factor complicating any assessment of COVID-related impact on this figure: improving editorial rigour. This time last year, around 9% of active drugs had not been updated for more than 12 months, whereas this year that figure is closer to 4%. The end result of the review which we conduct for many drugs which 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 suppressing this year's Active total. This can be confirmed by looking at the number of drugs moved to NDR in each year: in 2019, it was 3,170; whereas in 2020, it was up to 4,607. Without around 1,500 more drugs being taken out of the Active data set, our 2021 total might have been closer to 20,000 and posting an increase of 13.2%. The effects of editorial practice are unavoidable, and this should be borne in mind throughout this report when looking at absolute numbers. Fortunately, they have a systematic effect, so comparisons within each analysis remain perfectly valid.

Much like the real universe then, it seems that the pharma R&D universe continues to swell inexorably, and that not even evil alien invaders from the planet Corona can halt the expansion of its empire. But science fiction is littered with examples of federations and empires which grew bloated and became toxic (*Star Wars*, TV's *Blake's 7*). Is a bigger pharma R&D pipeline necessarily better?

To justify its ongoing expanding pipeline and the resulting increased costs, the pharma industry has to do one simple thing – produce more new drugs approved for use in patients. We will be analysing how well it did this through 2020 in detail in our follow-up supplement to this report focusing on the year's New Active Substance (NAS) launches. But early indications are that, despite the fact that there were initial delays to drug launches in the earlier part of the year, the pandemic did not have a noticeable effect on depressing new drug delivery, with NAS launches again exceeding 70. Coming on the back of two very successful years in 2018 and 2019, it seems that, despite the attack of the COVIDs, the pharma empire is still very much striking back.

Figure 1: Total R&D pipeline size, by year, 2001–21



Source: Pharmaprojects®, January 2021

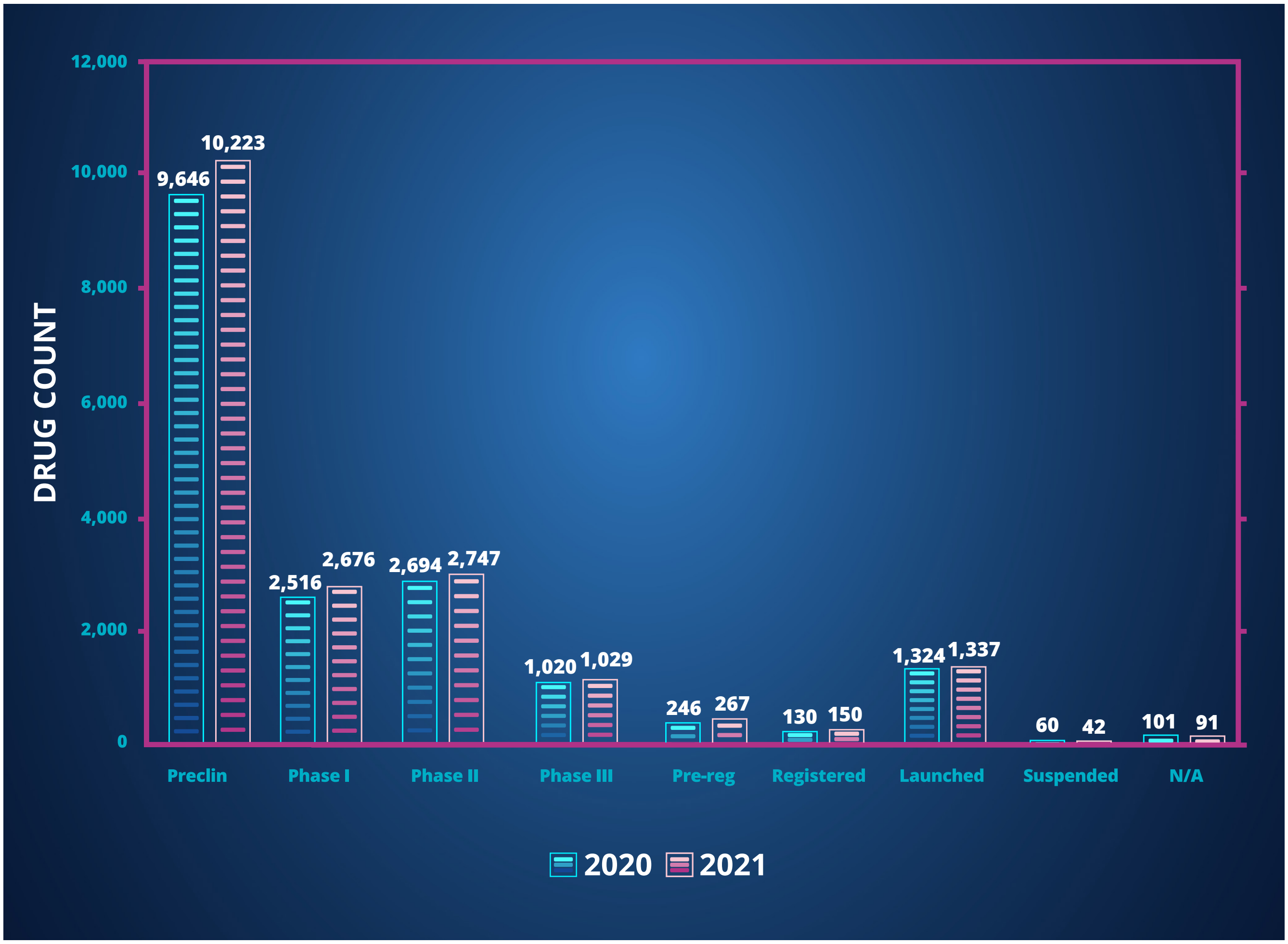
Into The Matrix: The 2021 Pipeline by Phase

Have clinical delays left R&D in cryosleep?

Let's break down those 18,582 drugs into how far up the evolutionary scale they have progressed. Figure 2 shows the pipeline divided by drug global status and once again compares numbers from January 2021 to those seen a year ago, before we had succumbed to the intergalactic plague we are currently battling. How well did the pharma stormtroopers fare in the face of the evil virus empire?

It's clear immediately that the vast majority of the growth in the pipeline came at the preclinical end of things. The number of drugs at this earliest stage of development rose this year to 10,223, up by 577, or a relatively modest 6.0% (the rate was 13.2% last year). Clearly, this is where most of the 'churn' happens; the majority of the 5,544 new drugs added will be at the preclinical phase, as will a large proportion of the Death Star-sized 4,744

Figure 2: Pipeline by development phase, 2021 versus 2020



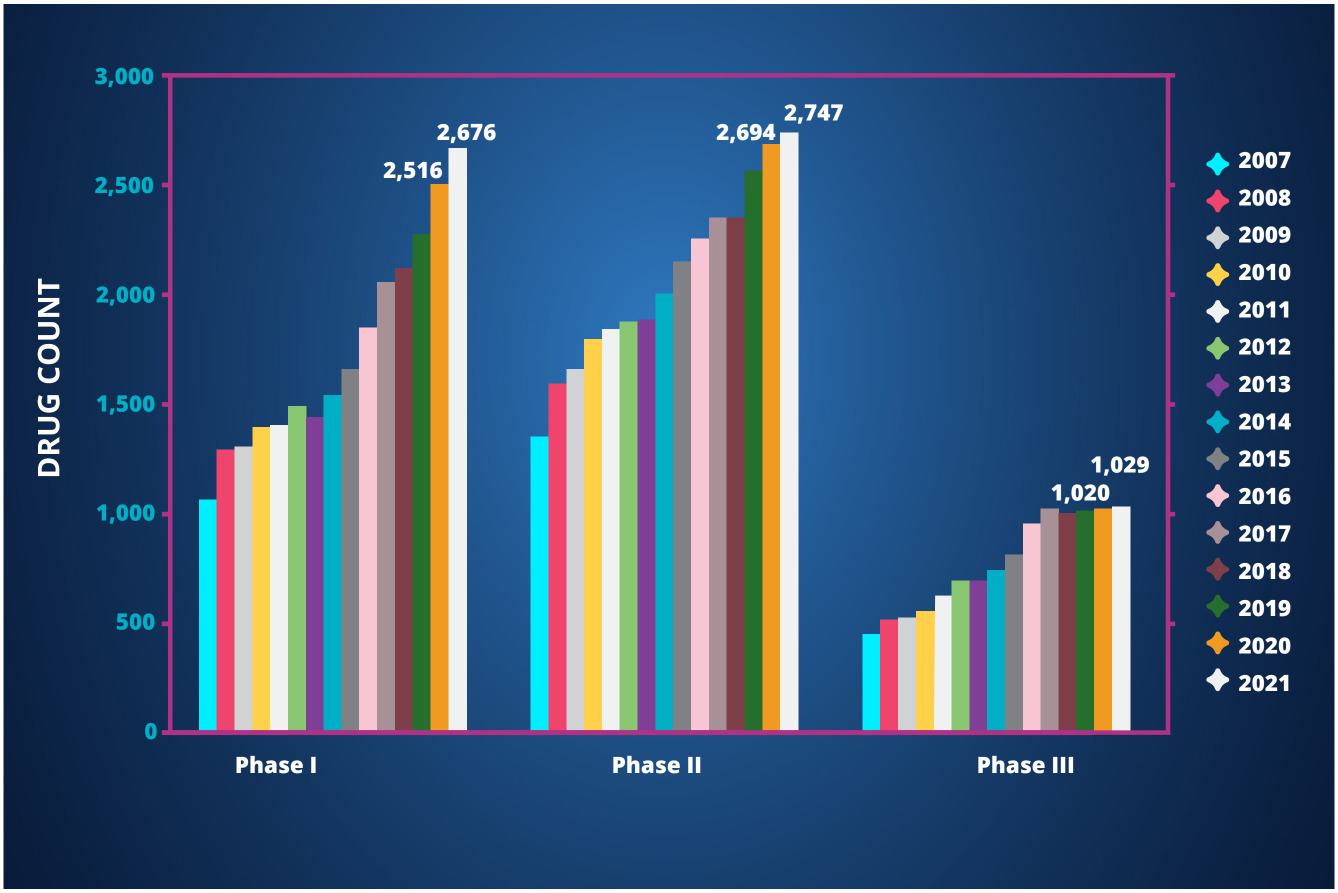
[N/A = not applicable and is applied to companion diagnostics prelaunch] / Source: Pharmaprojects®, January 2021 drugs which met *The Terminator* and were either confirmed as discontinued or moved to NDR status. So 2021's set of preclinical drugs will undoubtedly be a very different set to those from 2020. But it's good to see that the pandemic doesn't seem to have affected discovery as yet, although there could still be a delayed reaction as the effect of stay-at-home orders will inevitably slow down the pace of basic research to some degree.

As drugs progress down the development pathway through clinical trials, we see the increases in numbers start to taper off. While the growth in Phase I numbers is still substantial at 6.4%, it is only 2.0% at Phase II, and 0.9% at Phase III. This can be seen more clearly in Figure 3, which looks at clinical phase trends back to 2007. We can see that while Phase III has been stagnating for some time, the rises at Phase I and Phase II have definitely slowed compared to the previous couple of years.

It's hard to escape the suspicion that the coronavirus is having an effect here. There are something like >1,000 industry-sponsored trials in our sister service *Trialtrove* positively identified as impacted by COVID-19 – and we can assume quite a few more were also affected but there was no specific report of the delay (or report to link the delay to COVID). It's also likely that there would have been a reasonably large number of planned trials for 2020 which never got disclosed in the public domain and which were quietly postponed as well (particularly early-phase trials and those from private companies). Therefore, with a lot of trials quietly ejected from the airlock into deep space, might we be yet to see the impact of COVID-19 on clinical drug numbers? Might this play out over a few years, even if the pandemic is fixed this year? "Yes, that's definitely possible," says Andy Benson, Senior Director at *Trialtrove*. "Most of the impacted trials from 2020 are now either back up and running or terminated, but it (the COVID pandemic) could have a lingering impact on activity for sure."

There are also some encouraging data suggesting that the impact might not be as great as some might have feared. Taking Oncology as an example, *Trialtrove* actually reported more trial starts in 2020 than ever, with the figure of around 4,700 representing an increase of 9.0%, somewhat terminating the idea that R&D into other diseases has suffered as everyone focused on the virus. However, this does pale in comparison with Anti-Infective trial starts, which rose by 220%! The overall impression is that, rather than diverting research away from other diseases, the industry just *did a whole lot more*. And while there must inevitably be some impact from delays and diversions, there will also be positive effects which ripple out across the pharma R&D universe from a period of such an intense firing of the R&D thrusters. Just as the Second World War is believed to accelerated the space race and led to men on the moon in the 1960s, the pandemic has certainly turbocharged vaccine research, the positive effects of which will be felt for many years to come. Nonetheless, the number of drugs in clinical development will be a figure worth keeping a keen eye on over the next few years.

Figure 3: Clinical phase trends, 2007–21



Source: Pharmaprojects®, January 2021

> ***"Science is magic that works."***
> -Kurt Vonnegut

First Contact: Top Companies

Swiss duo take the top slots, but the rebel alliance of smaller companies gains further ground

A common trope of science fiction is a universe populated by large federations of disparate planets and peoples, some in competition, some co-operating, some invading and taking over others' worlds. This has in particular served the *Star Trek* franchise well for over 55 years, but crops up in *Star Wars* too, along with in literary works by luminaries such as Isaac Asimov and EE 'Doc' Smith. 2020 probably saw the pharma industry resemble the United Federation of Planets more closely than ever before, with unprecedented levels of co-operation and data sharing across companies, whom nonetheless are keeping one eye firmly on their own interests. So, let's move our analysis on to look at pharma's cast of characters, starting with its biggest companies – the multinational giants with empires of their own; the industry's Vulcans, Romulans and Klingons, if you like.

Guardian of the galaxy for the fifth year running is Novartis, which remains pre-eminent at the top of our table (Table 1). It posted a modest increase in its overall pipeline size, and once again originated the most drugs. It also was involved in the successful delivery of three further NASs to the market. Two of these were the result of a successful in-licensing strategy: capmatinib (Tabrecta), from a deal with Incyte in 2009, was brought to the market in Japan for non-small cell lung cancer; and it has taken rights in North America and certain European countries to BeiGene's tislelizumab, which the Chinese company has launched in its home territory for urothelial cancer and Hodgkin's lymphoma. It was also the originator of osilodrostat, which it divested to Recordati in 2019, the latter then going on to successfully bring it to market in the US and Europe for the treatment of Cushing's disease.

Novartis is joined at the top of the table this year by its compatriot Roche, up to number two on the back of three acquisitions during the year: Promedior, Foundation Medicine and Inflazome. But Roche's ascent cannot wholly be attributed to these relatively small takeovers, which added just 10 drugs between them, so we are seeing some genuine organic growth here. The two Swiss leviathans are some way ahead of the falling third-placed Takeda, although the Japan-based multinational held steady in terms of actual pipeline projects.

The highest climber in the top 10, and almost doubling its retinue of candidates, is AbbVie. Here, an acquisition is most definitely responsible, with the Illinois-based company completing its purchase of Allergan back in May 2020, in what was the year's biggest takeover. Elsewhere in the top 10, M&A was relatively muted: Novartis absorbed The Medicines Company, Takeda took over PvP Biologics, Bristol Myers Squibb acquired Forbius and MyoKardia, Merck & Co bought ArQule, Johnson & Johnson took TARIS Biomedical and Momenta Pharmaceuticals on board, and Sanofi acquired Synthorx and Principia Biopharma. Aside from ArQule, these acquisitions were pharma minnows, and notably Pfizer and AstraZeneca declined to venture beyond their own solar systems. Overall, though, and perhaps counterintuitively, we reported more mergers and acquisitions in 2020 than during the previous two years, with 142 such deals being done. Negotiations may not be taking place face-to-face so much, but the appetite of pharma's leading races to absorb inferior beings continued unabated.

Elsewhere in our top 25, Sanofi re-entered the top 10 after falling out of it last year following a pipeline audit. Fellow French company Servier was one of three new entries to the table this year, joined by Regeneron and CSL. These three companies appear at the expense of three firms which have dematerialized from the top 25 table, Lee's Pharmaceutical (down to number 28), Yuhan (down

Table 1: Top 25 pharma companies by size of pipeline

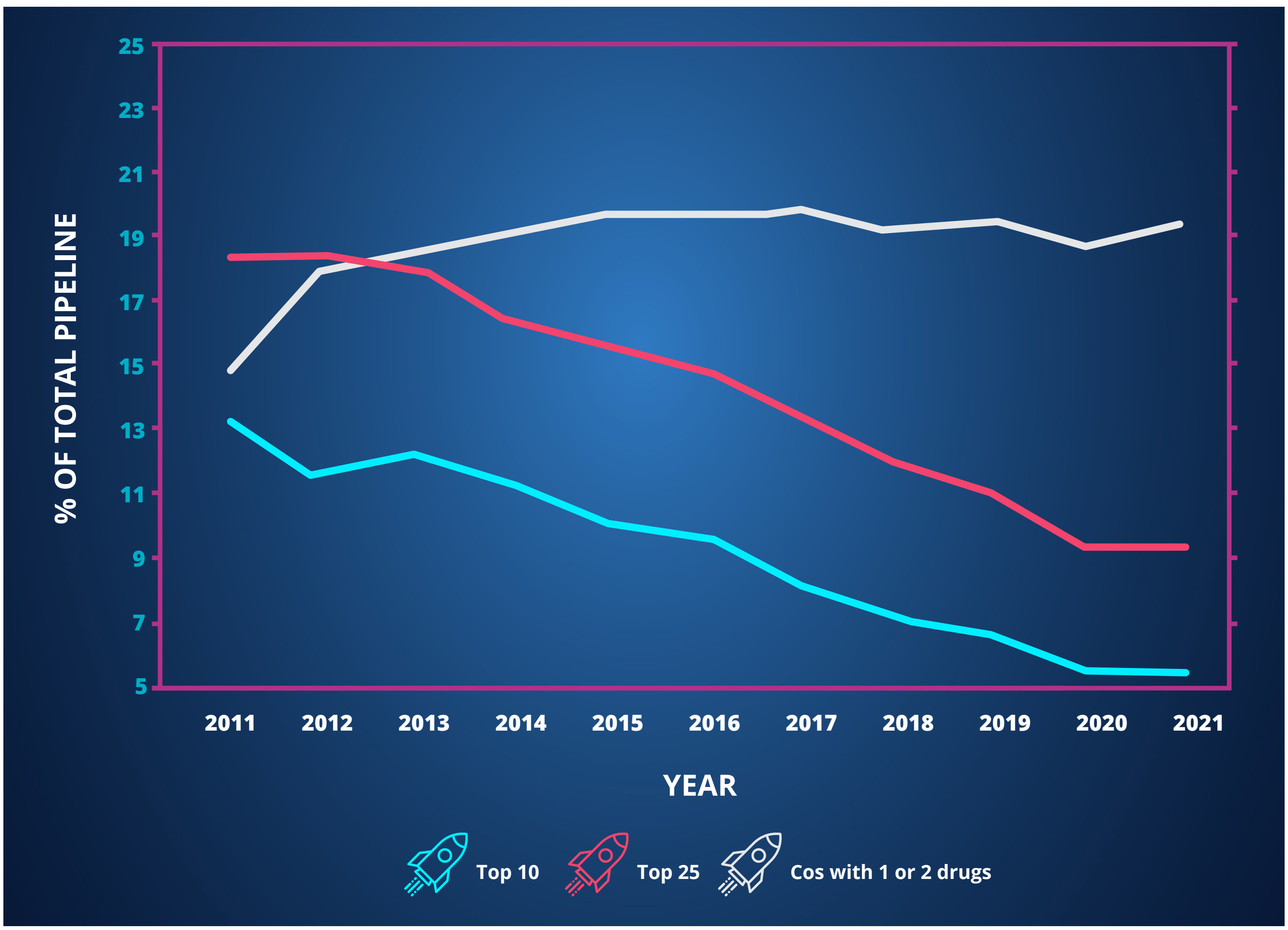
Position 2021 (2020)	Company v	No of drugs in pipeline 2021 (2020)	No of originated drugs 2021	Trend
1 (1)	Novartis	232 (222)	145	↔
2 (5)	Roche	227 (174)	137	↑
3 (2)	Takeda	199 (198)	86	↔
4 (3)	Bristol Myers Squibb	177 (189)	99	↔
5 (8)	Merck & Co	176 (157)	91	↑
6 (6)	Pfizer	170 (170)	113	↔
7 (4)	Johnson & Johnson	162 (182)	85	↓
8 (16)	AbbVie	160 (89)	64	↑↑
9 (7)	AstraZeneca	157 (164)	89	↔
10 (11)	Sanofi	141 (137)	71	↔
11 (10)	Eli Lilly	126 (143)	69	↓
12 (9)	GlaxoSmithKline	113 (144)	55	↓
13 (13)	Bayer	108 (93)	71	↔
14 (12)	Boehringer Ingelheim	97 (108)	63	↔
15 (14)	Otsuka Holdings	95 (91)	50	↔
16 (22)	Gilead Sciences	95 (73)	64	↑
17 (18)	Eisai	85 (84)	50	↔
18 (24)	Evotec	80 (70)	43	↑
19 (25)	Ligand Pharmaceuticals	78 (66)	44	↑
20 (17)	Daiichi Sankyo	78 (87)	45	↔
21 (15)	Amgen	77 (89)	53	↓
22 (20)	Astellas Pharma	76 (75)	43	↔
23 (30)	Servier	67 (58)	29	↔
24 (35)	Regeneron	64 (50)	39	↑
25 (28)	CSL Limited	64 (60)	41	↔

Source: Pharmaprojects®, January 2021

to 32), and the aforementioned acquiree, Allergan. Gilead Sciences is a high climber, fuelled somewhat by buying Immunomedics, and, to a lesser extent, Forty Seven.

In stark contrast to last year, the majority of companies (16 of 25) in the top 25 table are reporting larger pipelines now. Does that mean the trend of the power ebbing away from big pharma's Borg-like collective of giant companies, whose mantra might once have similarly been 'resistance is futile', has been reversed? The data in Figure 4 suggest not. This year, the stormtroopers of the top 25 companies originated 9.36% of all drugs, a decline from the 9.47% seen in 2020, although the rate of contraction has slowed. The same is true for the share contributed by the top 10, which stands at 5.27%, falling from 5.40%. The giant stars in the pharma sky continue to not burn quite so brightly. On the other side of the galaxy, the percentage of the overall pipeline contributed by the white dwarf companies with only one or two drugs in their pipeline increased again to 19.36%, although the trend here is pretty flat.

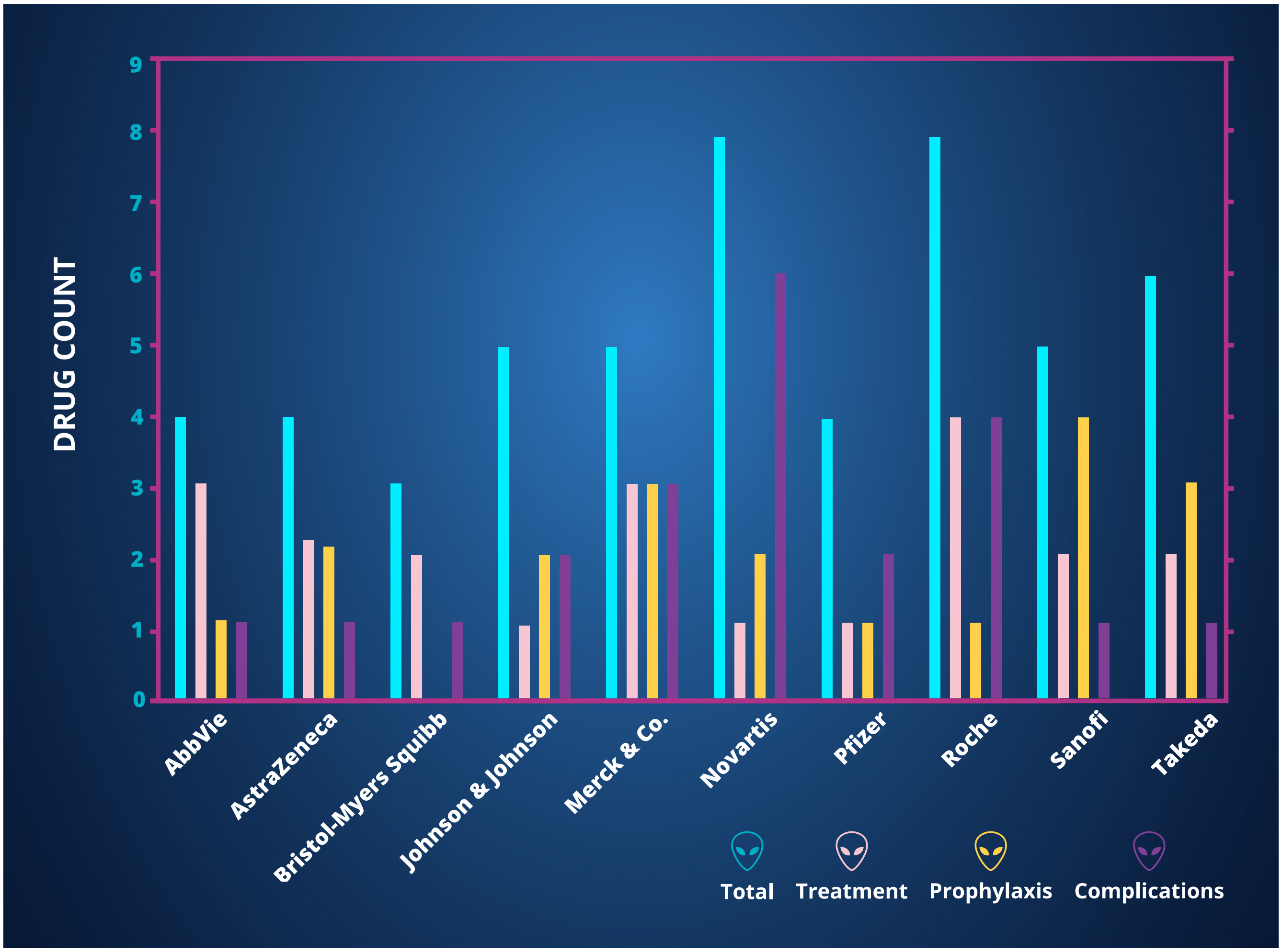
Figure 4: Share of the pipeline contributed by top 10 companies, top 25 companies, and companies with just one or two drugs, 2011–21



Source: Pharmaprojects®, January 2021

Who are the most fearsome warriors in the interspecies war against the virus? Figure 5 shows that all of the top 10 pharma companies have signed up to strike down the virus with great vengeance and furious anger (OK, not a sci-fi quote, but one lifted from *Pulp Fiction*) to varying degrees, with our Swiss top pair leading the way. The types of approaches are also broken down – note that some drugs can be classified in more than one category. Of course, two of these companies, Pfizer and AstraZeneca, have already delivered COVID-19 vaccines to a grateful world, with Johnson & Johnson expected to join them shortly, at the time of writing. Meanwhile, Novartis has the largest set of drugs for COVID-19 complications, with four of its six candidates being existing approved drugs being repurposed for this use. We'll be taking a deeper dive into the rapidly evolving world of the novel coronavirus in our section on disease trends later.

Figure 5: COVID-19 response from top 10 pharma companies



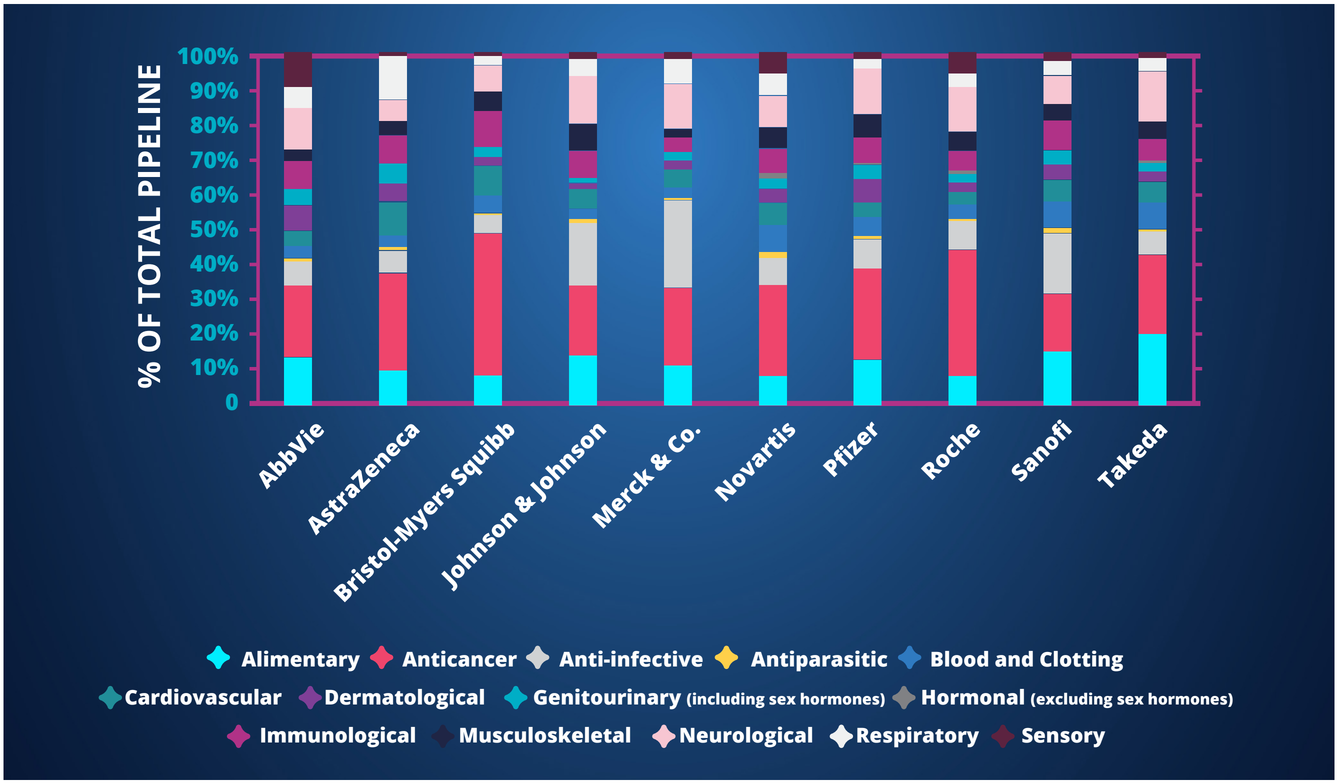
Source: Pharmaprojects®, January 2021

It's not surprising that all of the top 10 have piled into the brave new world of SARS-CoV-2, as the major pharma players continue to have broad interests, as we discovered last year with the new analysis of the top 10 companies by therapeutic area of interest, which was facilitated by our data remodelling enhancement which links each individual combination of company, disease, country and development status. At the time, I noted that the breadth of disease coverage which the big pharma companies still had was a little surprising in an age when we are told that firms prefer to focus in on a few key areas of expertise. Has the coronavirus shifted the needle on this at all?

As Figure 6 shows, six of the top 10 still have some activity in every single therapeutic area, including even the very smallest category, Antiparasitics. The other four only have an omission in a single area, Hormonal products, which is the second smallest anyway. Cancer remains the largest area of interest for all of the top 10 aside from Merck & Co, which majors in Anti-Infectives, as it did last year. There certainly are some companies whose Anti-Infective bar has noticeably widened this year, notably AstraZeneca and Bristol Myers Squibb, the latter of which now has 18 drugs, up from seven last year. The effect that the virus has had on anti-infective research overall we'll come back to in the next section.

In terms of the total number of companies involved in development, it's a similar story to that seen with the total number of drugs – continued expansion, but at a somewhat slower rate. There are 5,099 companies involved in pharma R&D as of January 2021, an increase of 283, or 5.9%. This compares unfavourably with 2020's supernova-like 11.4% expansion, but easily beats the percentage increases seen in the previous two years. As usual, this modest increase masks considerable churn. A record-breaking 1,055 new companies were added

Figure 6: Disease focus areas of the top 10 pharma companies



Source: Pharmaprojects®, January 2021

to our database – so over a fifth of all companies were newly identified in 2020. This knocks the previous year's 809 into hyperspace. It's possible that the high profile for pharma throughout the year provided fertile ground for start-ups. It also means that a net of 772 firms fell out of pharma time and space, far exceeding the equivalent figure of 316 from 2020, although again improved editorial practices may have had a considerable bearing on this number. Most of these companies have disappeared quietly as they have ceased to provide new information on their candidates, rather than definitively having imploded. Just as in *Alien*, in the pharma space, no-one can hear you scream.

However, this explosive expansion in new companies is surprisingly not reflected in increases in the number of really small firms we report this year. There are 733 companies with two drugs in their portfolio, down two from the 2020 figure, while the number of companies with a single drug is exactly the same – 1,849. It therefore follows that if the contribution to the overall pipeline of companies with one or two drugs has increased, as we saw in Figure 4, this must be due to declining numbers in larger firms' pipelines, since the actual number of drugs these pharma nanites contribute is almost exactly the same.

Figure 7: Total number of companies with active pipelines, 2001–21

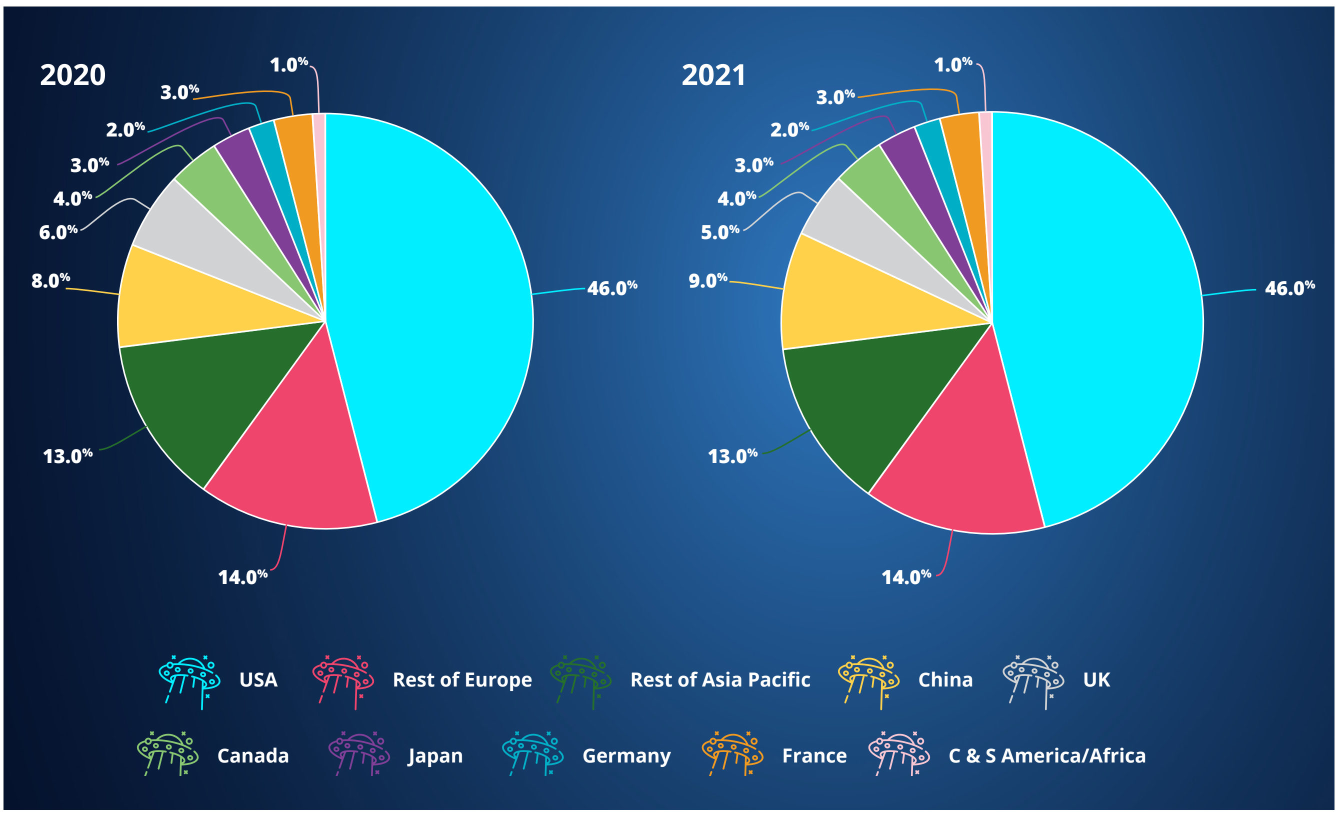
Source: Pharmaprojects®, January 2021

Data on the location of company HQs hasn't changed that much from 2020 to 2021. In Figure 8, the only shift is a further 1% increase in the contribution of companies based in China, at the expense of the UK. But the actual number of Chinese-based companies rose by an impressive 23% across the year to 522, adding 94, on the back of an increase of 121 in the previous year. There can be no doubt that the Chinese pharma R&D universe is expanding at an impressive rate. It's now in second place nationally by some distance, trailing only the US.

Although 46% of companies are headquartered in the US, an even greater proportion of drugs have some US development. Figure 9 shows that 10,260 of our 18,582 candidates – or 55% – have some US development reported. Strikingly, a sixth of all active candidates report development in China now, something which would have been unthinkable even a decade ago. The UK remains the premier country in Europe where drugs are being tested, with Germany just edging out France into second place. The Japanese market remains a huge, but somewhat distinct, environment, with only 7% of active drugs having current R&D reported there.

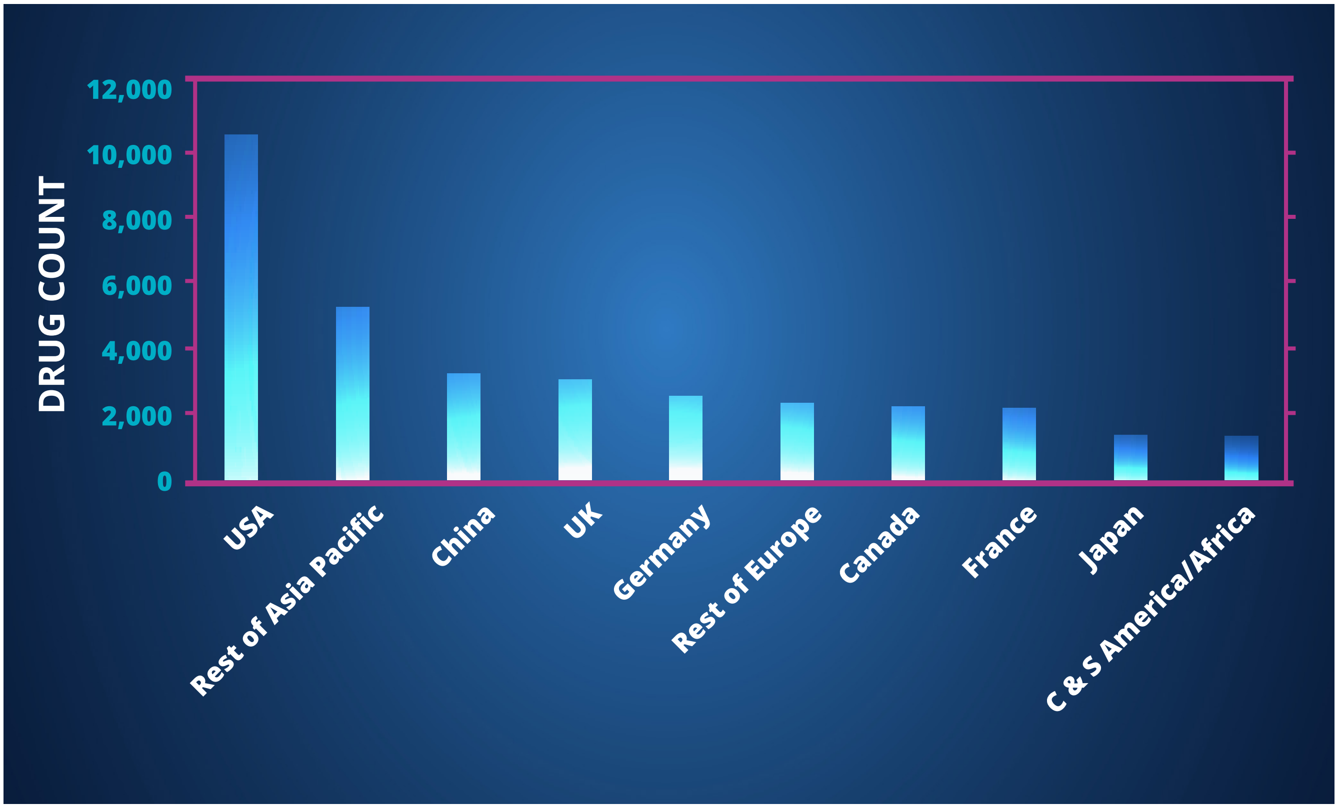
So, our section on companies again seems to suggest a pharma industry in rude health. More companies than ever before, more new companies than ever before, and with the leading companies having broad therapeutic interests. It has no doubt been a turbulent year for many firms, with clinical trial delays, and lockdowns preventing some staff from attending their labs. But the industry's response has been pretty robust. Perhaps it had been reading the famous front cover of Douglas Adams' fictional *The Hitchhiker's Guide to the Galaxy*: 'Don't Panic'!

Figure 8: Distribution of R&D companies by HQ country/region, 2020 and 2021



Source: Pharmaprojects®, January 2021

Figure 9: Where is R&D actually occurring?



Source: Pharmaprojects®, January 2021

"Science, my lad, is made up of mistakes, but they are mistakes which it is useful to make, because they lead little by little to the truth."
- Jules Verne, Journey to the Centre of the Earth

Warp Factor Two: Top Therapies

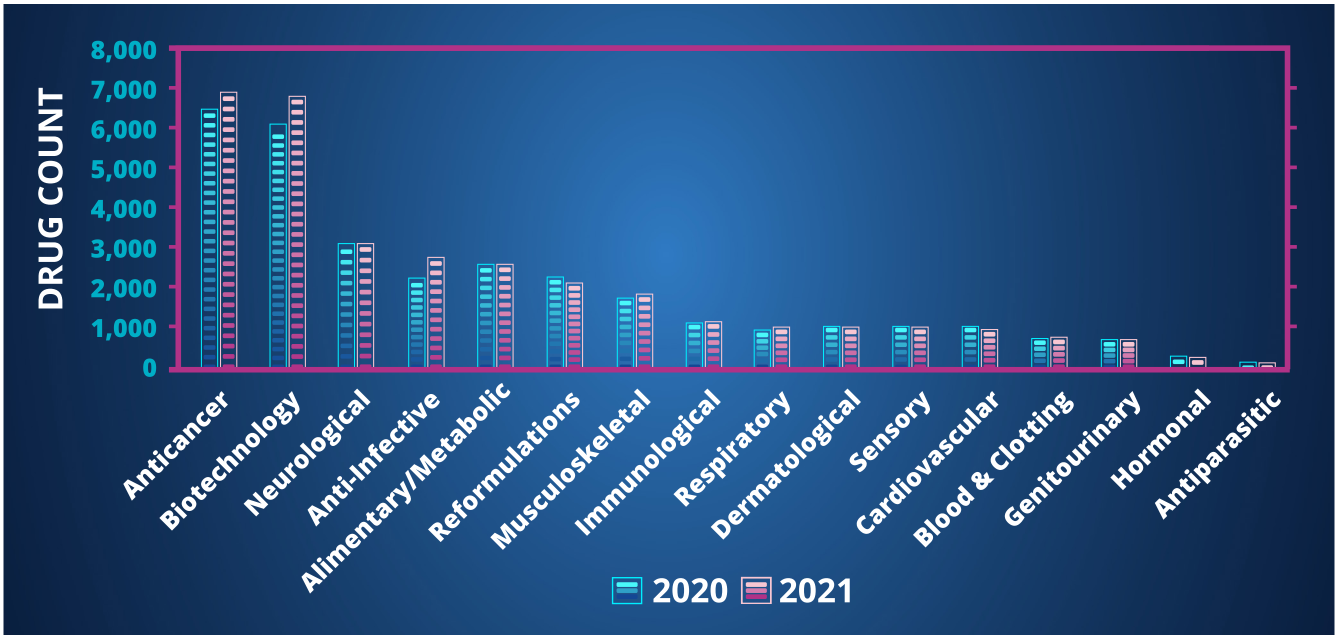
Pharma fights to repel the alien coronavirus invasion

As we move on to look at trends for therapeutic areas and diseases, the novel coronavirus will inevitably raise its ugly head repeatedly. It's worth remembering that pandemics are nothing new and have plagued the human race – if you pardon the pun – throughout history, from at least as soon as humanity developed farming and began to associate in communities, around 10,000 years ago. The earliest recorded pandemic occurred at the time of the Peloponnesian War around 430 BC, when around two thirds of the population of Athens died. The Middle Ages were scarred by outbreaks of the bubonic plague, and a recurrence in London in 1665 killed 20% of the city's population. Then there is the avian 'Spanish' flu outbreak of 1918–19, which famously killed more people than the First World War, around 50 million worldwide. Interestingly, it disappeared almost as quickly as it had spread, as herd immunity developed. By mid-1920, most people had either recovered from the illness, or already died from it.

Of course, plagues and pandemics have long been fertile source material for a certain strain of apocalyptic science fiction. A BBC TV series, *Survivors*, ran for three series from 1975 to 1977, and featured a plague which coincidentally originated in China, but had an horrific 99.9% fatality rate. Notable examples from literature include Michael Crichton's *The Andromeda Strain* (also made into a film), where the pathogen is of extra-terrestrial origin, and *Blindness* by Nobel laureate José Saramago. There is also the subgenre of SF/horror where infections lead to people turning into zombies or vampires. However horrendous the past year has been, fiction can always outdo reality.

Beginning with a look at trends in the broad therapeutic areas of drug development, the COVID effect can immediately be seen in Figure 10. Anti-Infectives post by far the biggest percentage increase of any group, up an astronomical 22.4%,

Figure 10: The R&D pipeline by therapy group, 2020 and 2021



Source: Pharmaprojects®, January 2021

pretty much entirely due to the development of new therapies and vaccines against COVID, as we'll see later. This also is in contrast to the 2020 trend, where Anti-Infectives were actually seen to be in decline. But anti-infective research is still dwarfed by the leading therapeutic area, anticancers. Despite the world's eyes being diverted elsewhere, the pharma oncology franchise grew to 6,961 drugs in 2021, and expanded by a further 7.0%, outpacing the overall rate of pipeline growth once again. However, this is just below half the rate seen in 2020, suggesting that the inexorable rise of anticancer R&D was perhaps somewhat dented by resources redeployed against the pandemic.

Biotechnology drugs, while not strictly speaking a 'therapeutic' area, are included in this analysis, and their group grew by an even more impressive 11.1%. Elsewhere, though, the other biggest therapeutic area counts were almost entirely flat: Neurologicals up just six drugs to 3,063, and Alimentary/Metabolics posting exactly the same number of candidates as last year, 2,599. These classes grew by 10.2% and 8.0%, respectively, last year. It's always worth noting here that drugs can be counted more than once in this graph, as many cross a number of therapeutic areas (for example, antiarthritic drugs could be considered both musculoskeletal and immunological). This is particularly true of Anticancers, where almost half of drugs (48.8%) also fit into the Biotechnology group.

Despite a slowing in its expansion rate this year, though, cancer continues to exert a Vulcan death grip-like hold on pharma R&D. Figure 11 shows that the proportion of the pipeline which is in development for cancer has continued to increase, despite the pandemic, with 37.5% of all drugs having an oncological focus. The 2020s should really be the decade where we are able to say *"Hasta la vista, baby"* to more tumours than ever before.

Figure 11: Proportion of the pipeline which is in development for cancer, 2010–21

Source: Pharmaprojects®, January 2021

Table 2 breaks down these solar systems of therapeutic areas into the individual planets of the 240 therapeutic categories. For the third year in a row, the Anticancer, immunological category sits at the summit, with another sizeable increase in its gravitational pull, with 8.1% more drugs in its pipeline than a year ago. Again, the rate of expansion has slowed compared to the previous year. The other more general anticancer category – Anticancer, other – sticks at number two, put we can see that the hyperdrive of immuno-oncology is causing the leading category to put further space between the top two. At three, there's a further sizeable regeneration of the gene therapy franchise, of which more in a moment. The highest climber is, unsurprisingly, the general antiviral category, which leaps up from number 28 into the top five, with a supermassive 126% increase in its drug count. Just behind it are anti-infective prophylactic vaccines. We'll be digging into the new COVID-19 market in a bit more detail when we get to our disease-level analysis.

Meanwhile, it's a top 10 debut for the Cellular therapy, chimaeric antigen receptor, or CAR-T, category, which only entered the top 25 for the first time last year. As with Figure 13, drugs can appear in more than one category, and the rise in CAR-T therapies will certainly have been a big contributor to the table leader's increase. Further down the table, the general respiratory category jumps into the top 20, fuelled by a plethora of new and repurposed drugs to treat the inflammatory lung effects of serious COVID-19 infection. The final two entries to this year's top 25 chart are both centred around cell therapy, which continues to make advances even away from the CAR-T revolution. Dropping out of the table this year are Biosimilar; Dermatological; Metabolic and enzyme disorders; and Reformulation, fixed dose combinations.

"Space is big. Really big. You just won't believe how vastly, hugely, mindbogglingly big it is. I mean, you may think it's a long way down the road to the chemist, but that's just peanuts to space."
Douglas Adams, The Hitchhiker's Guide to the Galaxy

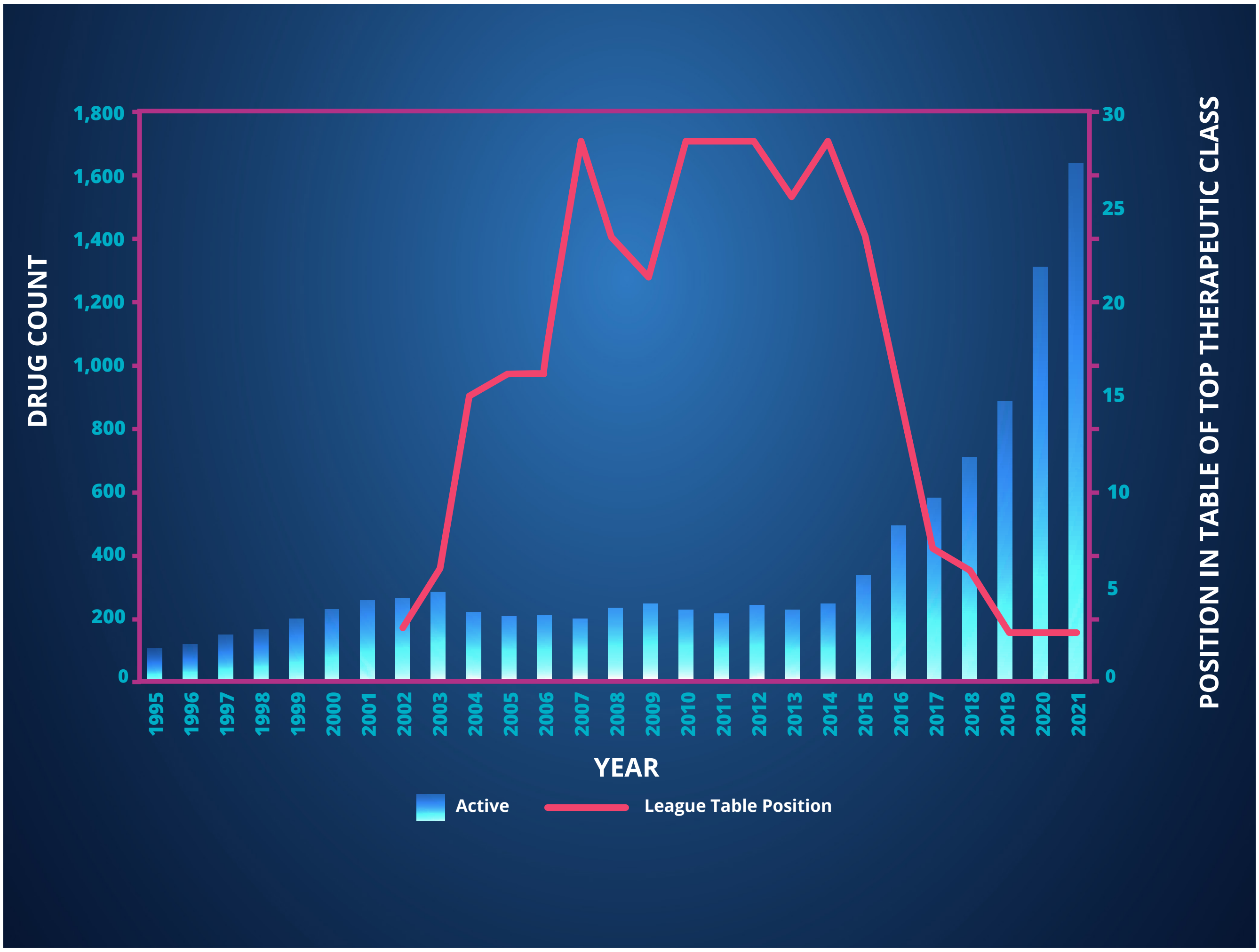
Table 2: Top 25 Therapeutic Categories

Position 2021 (2020)	Therapy	No of active compounds 2021 (2020)	Trend
1 (1)	Anticancer, immunological	3,712 (3,434)	↑
2 (2)	Anticancer, other	2,680 (2,510)	↑
3 (3)	Gene therapy	1,589 (1,273)	↑
4 (4)	Monoclonal antibody, other	1,136 (1,009)	↑
5 (28)	Antiviral, other	858 (380)	↑↑
6 (6)	Prophylactic vaccine, anti-infective	843 (698)	↑
7 (5)	Ophthalmological, other	781 (756)	↔
8 (7)	Neurological	781 (666)	↑
9 (10)	Anti-inflammatory	639 (529)	↑
10 (14)	Cellular therapy, chimaeric antigen receptor	612 (491)	↑
11 (8)	Antidiabetic	569 (589)	↔
12 (11)	Monoclonal antibody, humanized	555 (508)	↑
13 (9)	Immunosuppressant	542 (544)	↔
14 (12)	Musculoskeletal	521 (504)	↔
15 (18)	Monoclonal antibody, human	494 (448)	↑
16 (15)	GI inflammatory/bowel disorders	482 (488)	↔
17 (13)	Reformulation, other	470 (492)	↓
18 (17)	Cognition enhancer	459 (466)	↔
19 (23)	Hepatoprotective	453 (418)	↑
20 (35)	Respiratory	446 (303)	↑↑
21 (16)	Cardiovascular	444 (468)	↓
22 (27)	Cellular therapy, stem cell	428 (391)	↑
23 (19)	Analgesic, other	427 (448)	↓
24 (21)	Neuroprotective	426 (421)	↔
25 (30)	Cellular therapy, other	419 (350)	↑

Source: Pharmaprojects®, January 2021

This year, we're able dig a little deeper into the field of gene therapy, thanks to a new Cell and Gene Therapy dashboard produced by Informa Pharma Intelligence. We've seen a further significant increase in the overall number of drugs in development using this technique this year, which is further highlighted in Figure 12. It's at 1,589 projects now, up almost a quarter (24.8%) in a single year, and has retained its position at number three in the table of top therapeutic categories. Gene therapy has had an even bigger return than the Jedi did, having resurrected its fortunes from its late noughties doldrums. The increase is generated by two types of gene therapy: ex vivo gene therapy, where cells are modified outside of the body before being reintroduced; and in vivo gene therapy, where the genetic manipulation occurs inside the body. For the latter, the vector used to deliver the gene is becoming increasingly important, and is something the *Pharmaprojects* Analyst team is often asked about.

Figure 12: The ongoing rise of gene therapy



Note: tracking of therapeutic category league tables only began in 2002.

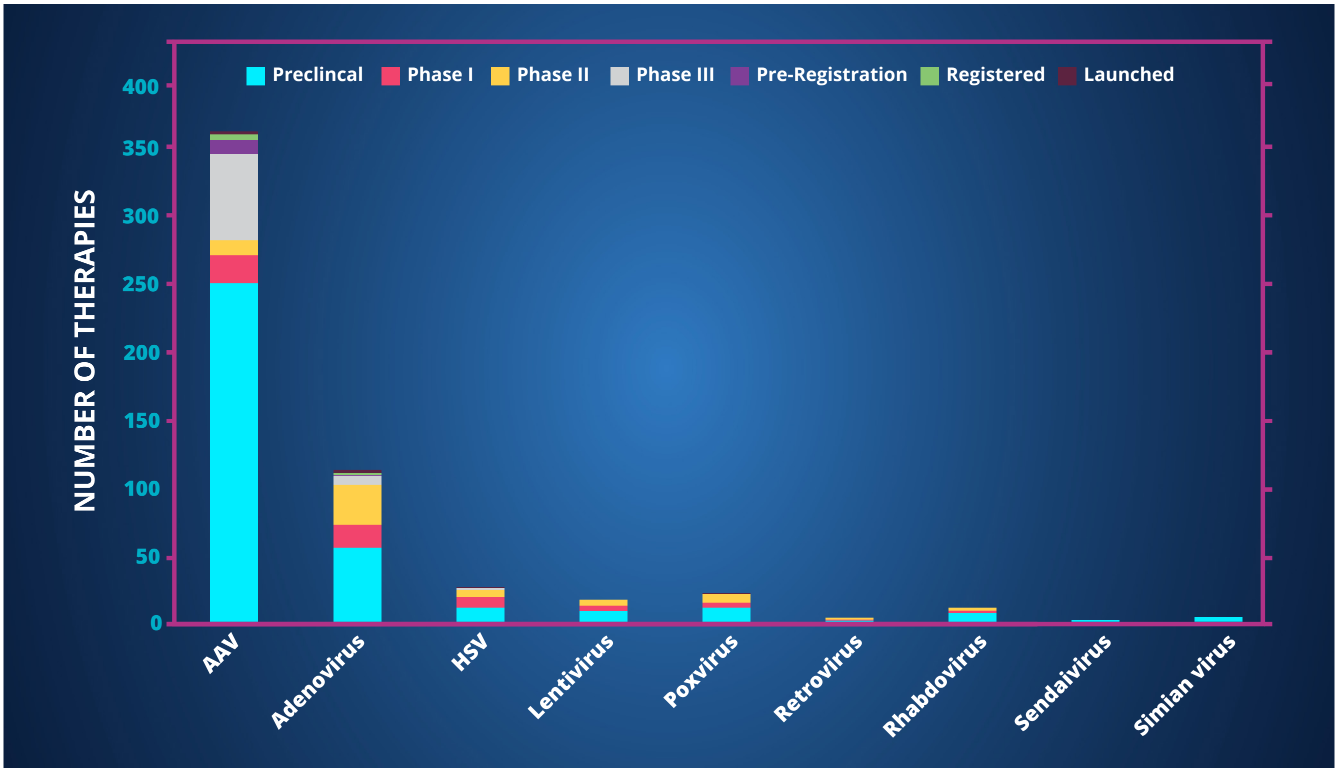
Source: Pharmaprojects®, January 2021

Due to new indexing applied on our gene therapy dashboard, we're able to provide robust granular analyses to the new world of gene therapy. For instance, we can now slice the virally delivered gene therapies by the type of viral vector used, which is what we can present in Figure 13, which also breaks each class down by phase of development.

This shows that the various subtypes of adeno-associated virus, or AAV, are by far the pre-eminent choice of gene therapy developers, with nearly 350 candidates using this technique. AAV is a popular choice as it is non-pathogenic in humans, and the level of exposure to some of the many wild-type AAV subtypes among the general population is sufficiently low that patients are less likely to develop potentially disastrous antibodies against the vector itself. This is less true for the second-placed adenovirus. But our data show that there are other viral vectors beyond these two major classes being investigated, including Herpes simplex viruses, poxviruses, lentiviruses and rhabdoviruses.

Let's now teleport straight to the top 25 individual diseases against which drugs are currently being developed, which you'll find in Table 3. Breast cancer remains the industry's leading target, but interestingly the number of actual candidates has fallen for the first time this year, although only by 4%. Meanwhile, its nearest rival, non-small cell lung cancer, is up 5% at number two, followed by almost unchanged pipeline sizes for the number three and four entries, colorectal and pancreatic cancers. But it's the number five which is most striking. Beaming straight in is a disease for which we had not even yet created an indication term at the start of 2020, when for most it seemed like an alien from a distant planet. We've never had a disease go from a standing start to warp factor 10 so quickly, so its appearance there is a measure of

Figure 13: Viral vectors used in gene therapy



Source: Pharmaprojects®, January 2021

Table 3: Top 25 diseases/indications

Position 2021 (2020)	Disease	No of drugs 2021 (2020)	Trend
1 (1)	Cancer, breast	886 (924)	↓
2 (2)	Cancer, lung, non-small cell	746 (710)	↑
3 (3)	Cancer, colorectal	653 (640)	↔
4 (4)	Cancer, pancreatic	570 (563)	↔
5 (-)	Infection, coronavirus, novel coronavirus	553 (-)	↑↑
6 (5)	Cancer, ovarian	518 (519)	↔
7 (6)	Cancer, prostate	481 (486)	↔
8 (7)	Cancer, brain	460 (479)	↔
9 (8)	Alzheimer's disease	436 (459)	↓
10 (9)	Arthritis, rheumatoid	435 (454)	↓
11 (12)	Cancer, leukaemia, acute myelogenous	430 (404)	↑
12 (10)	Cancer, melanoma	423 (440)	↔
13 (11)	Diabetes, Type 2	418 (434)	↔
14 (13)	Cancer, myeloma	409 (393)	↔
15 (14)	Cancer, liver	382 (357)	↑
16 (15)	Cancer, gastrointestinal, stomach	358 (354)	↔
17 (16)	Cancer, head and neck	357 (354)	↔
18 (-)	Infection, coronavirus, novel coronavirus prophylaxis	347 (-)	↑↑
19 (20)	Cancer, lymphoma, non-Hodgkin's	344 (315)	↑
20 (21)	Non-alcoholic steatohepatitis	340 (309)	↑
21 (17)	Parkinson's disease	340 (345)	↔
22 (18)	Psoriasis	315 (330)	↔
23 (-)	COVID-19 complications	266 (-)	↑↑
24 (19)	Pain, nociceptive, general	264 (244)	↑
25 (23)	Asthma	260 (255)	↔

Source: Pharmaprojects®, January 2021

the earth-shattering effect the disease has had in such a short time. Going from zero drugs to over 550 represents a phenomenal response by Earth's defence forces to this particular invasion. And that's only part of the story, as vaccines and treatments for the prophylaxis of the virus also materialise from nowhere at number 18, with drugs for the treatment of COVID-19 complications beaming in at number 23. We'll undertake a more forensic examination of planet COVID in a minute.
Away from the pandemic, cancer continues to dominate, and still has 14 of the top 20 slots, the same as last year. Whereas most of the solid tumours posted similar numbers to those seen in 2020, those for blood-based cancers in the top 25 had more significant increases: acute myelogenous leukaemia is up 6.4% at number 11, and non-Hodgkin's lymphoma expands by 9.2% at number 19. In a chart with few other climbers, non-alcoholic steatohepatitis stands out as another indication continuing to advance.

In years with larger overall pipeline expansions, it was very unusual to see indications whose pipeline size actually declined. But this year, with only a 4.76% overall growth rate, there are some diseases for which there are fewer drugs in development in 2021 than there were in 2020. I already noted a decline for breast cancer, and in oncology, it's joined by another tumour type, brain cancer. Away from cancer, Alzheimer's disease, that perennial conundrum which seems harder to solve than faster-than-light space travel, falters again, falling by 4.4%, and type 2 diabetes also dips down with a 3.8% decline. The entry of the three new COVID-related indications pushes out renal cancer, neuropathic pain and Crohn's disease from this year's table.

One of the interesting new analyses we were able to introduce last year thanks to our enhancement linking disease, company and country was an examination of regional variations of R&D by disease, and Table 4 recreates that graphic using 2021 data. Once again, it reveals some intriguing differences. The fact that the novel coronavirus only appears once in any of the geographic top eights, in the US, where it is even higher at number three, shows how US-centric the R&D response to the pandemic has been. Elsewhere, rheumatoid arthritis manages a top three showing throughout Europe and in South America, while type 2 diabetes maintains a strong presence in the top eight in Asian countries, Europe and South America, as well as in Africa. Africa, as last year, differs the most from the international chart, with much evidence of its own regional priorities: HIV/AIDS, tuberculosis and haemophilia. Meanwhile, cancer has a straight run in Canada, the UK and Oceania.

Table 4: 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	Asthma	Haemophilia A	Infection, tuberculosis	Haemophilia B
Asia	Cancer, breast	Cancer, lung, non-small cell	Cancer, gastrointestinal, stomach	Diabetes, Type 2	Cancer, liver	Cancer, pancreatic	Cancer, myeloma	Cancer, renal
Canada	Cancer, breast	Cancer, lung, non-small cell	Cancer, colorectal	Cancer, leukaemia, acute myelogenous	Cancer, myeloma	Cancer, ovarian	Cancer, gastrointestinal, stomach	Cancer, renal
China	Cancer, lung, non-small cell	Cancer, breast	Cancer, gastrointestinal, stomach	Cancer, liver	Diabetes, Type 2	Cancer, myeloma	Cancer, pancreatic	Cancer, leukaemia, acute myelogenous
EU	Cancer, breast	Cancer, lung, non-small cell	Arthritis, rheumatoid	Cancer, ovarian	Cancer, leukaemia, acute myelogenous	Diabetes, Type 2	Cancer, myeloma	Cancer, renal
Europe, non-EU	Cancer, lung, non-small cell	Cancer, breast	Arthritis, rheumatoid	Diabetes, Type 2	Colitis, ulcerative	Cancer, ovarian	Cancer, gastrointestinal, stomach	Cancer, renal
Japan	Cancer, lung, non-small cell	Cancer, breast	Diabetes, Type 2	Cancer, gastrointestinal, stomach	Cancer, leukaemia, acute myelogenous	Cancer, myeloma	Cancer, liver	Cancer, renal
Oceania	Cancer, breast	Cancer, lung, non-small cell	Cancer, colorectal	Cancer, myeloma	Cancer, leukaemia, acute myelogenous	Cancer, renal	Cancer, ovarian	Cancer, pancreatic
South America	Cancer, breast	Cancer, lung, non-small cell	Arthritis, rheumatoid	Diabetes, Type 2	Cancer, prostate	Cancer, gastrointestinal, stomach	Asthma	Cancer, renal
UK	Cancer, breast	Cancer, lung, non-small cell	Cancer, colorectal	Cancer, ovarian	Cancer, gastrointestinal, stomach	Cancer, renal	Cancer, leukaemia, acute myelogenous	Cancer, myeloma
USA	Cancer, breast	Cancer, lung, non-small cell	Infection, coronavirus, novel coronavirus	Cancer, pancreatic	Cancer, leukaemia, acute myelogenous	Cancer, ovarian	Cancer, myeloma	Cancer, colorectal

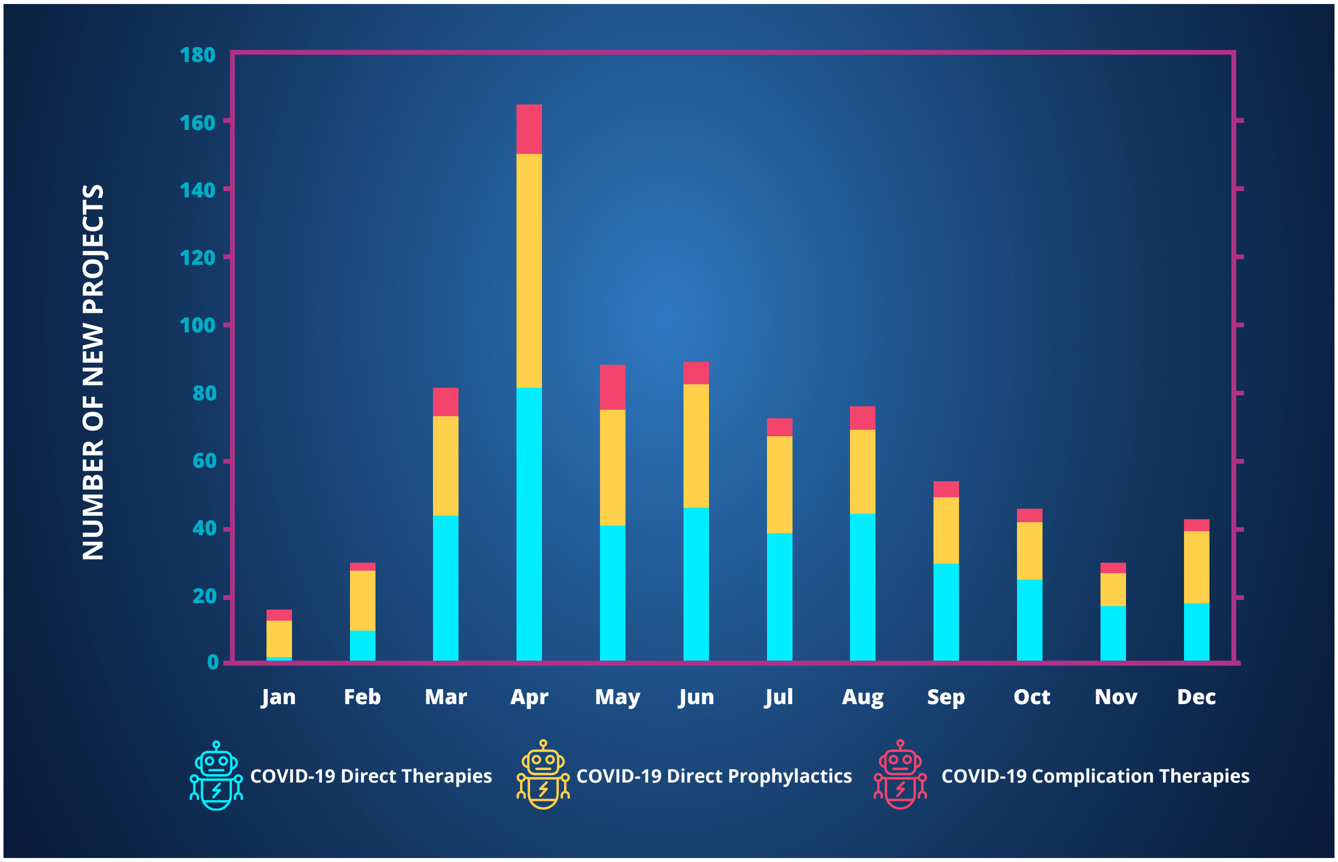
KEY	Cancer	Ailmentary/ Metabolic	Musculoskeletal	Respiratory	Infectious Disease	Blood & Clotting

Source: Pharmaprojects®, January 2021

So, let's now take a deeper dive into the invading army of the SARS-CoV-2 drugs and vaccines which have turned pharma R&D on its head over the past 12 months. As noted earlier, we have created three new indications in response to the emerging pandemic: Infection, novel coronavirus, which covers antivirals and other drugs treating the infection itself; Infection, novel coronavirus prophylaxis, featuring agents primarily designed to prevent infection or disease, which are mainly vaccines and MAbs; and COVID-19 complications, where you will find drugs which treat the numerous effects of the disease but not the virus itself, which are primarily anti-inflammatories or other agents to control the cytokine storm. Many of the latter are old, launched drugs which are being repurposed and resurrected for today, thus this field is perhaps the *Jurassic Park* of anti-pandemic R&D. Table 4 reports 553 drugs in the first class, 347 in the second, and 266 in the third. Not bad from a standing start. However, it's worth noting that some agents may be classified under more than one category; for example, monoclonal antibodies, which might be used therapeutically and prophylactically. Overall, the total number of active anti-COVID agents in development comes in at 1,012. A full 5.4% of the pipeline is for a disease virtually unheard of a year ago – that is some mobilization of the troops!

Just how quickly was this extraordinary response mounted? Figure 14 shows how many of each class of agent were added to the pipeline each month (note the earlier caveat that some programmes could cross classes). This shows an extremely rapid fightback against the COVID evil empire, with newly

Figure 14: Emergence of new treatments, vaccines and supportive therapies for SARS-CoV-2 during 2020



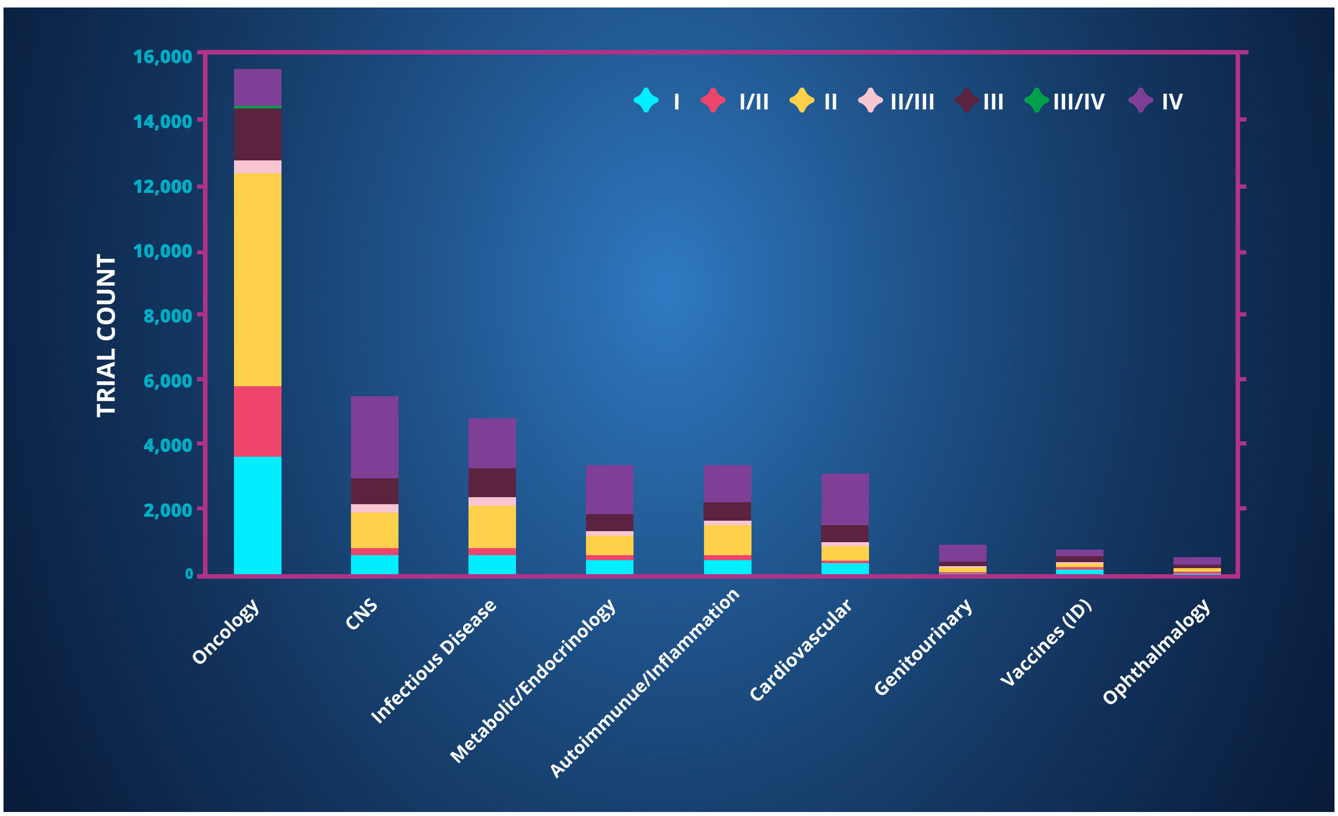
Source: Pharmaprojects®, January 2021

identified therapies, prophylactics and complication therapies peaking in April, around the time of the peak of the first wave of the pandemic in Europe (the picture in the US has been more complex). As much of the world, or the Northern Hemisphere at least, struggles with a much worse second or third wave this winter, there doesn't seem to have been a second wave of new drugs and vaccines – perhaps because the need is so urgent that if companies hadn't responded immediately, they might have missed the boat somewhat. That being said, the very end of the year certainly witnessed an uptick.

We are all hoping for a Close Encounter of the Vaccine Kind at some point during 2021. Of the six vaccines currently being administered around the world, all began development during that first peak, but even the early start doesn't really explain just how the industry managed to pull off such an amazing feat of bringing vaccines through development for widespread use in such a short time. It's almost as though R&D was taking place in a parallel universe where time runs at a different rate (another common sci-fi trope). It's an extraordinary achievement.

In all the cacophony about vaccines, one could be forgiven for thinking work on therapeutics had run aground, but, as we saw, therapeutics outnumber prophylactics by a warp factor of around 1.5. Around half of these are small molecule antivirals, of which almost 200 are not reformulations, so considerable work is under way, with around 50 in Phase II or III trials at the time of writing. It does seem likely that direct-acting antivirals or combinations thereof will have a future role to play in checking this devastating disease, just as they have done with other viral scourges such as HIV and hepatitis C. This view that we shouldn't be putting all of our eggs in the vaccine basket is shared by

Figure 15: Ongoing clinical trials, by therapeutic area



Source: Pharmaprojects®, January 2021

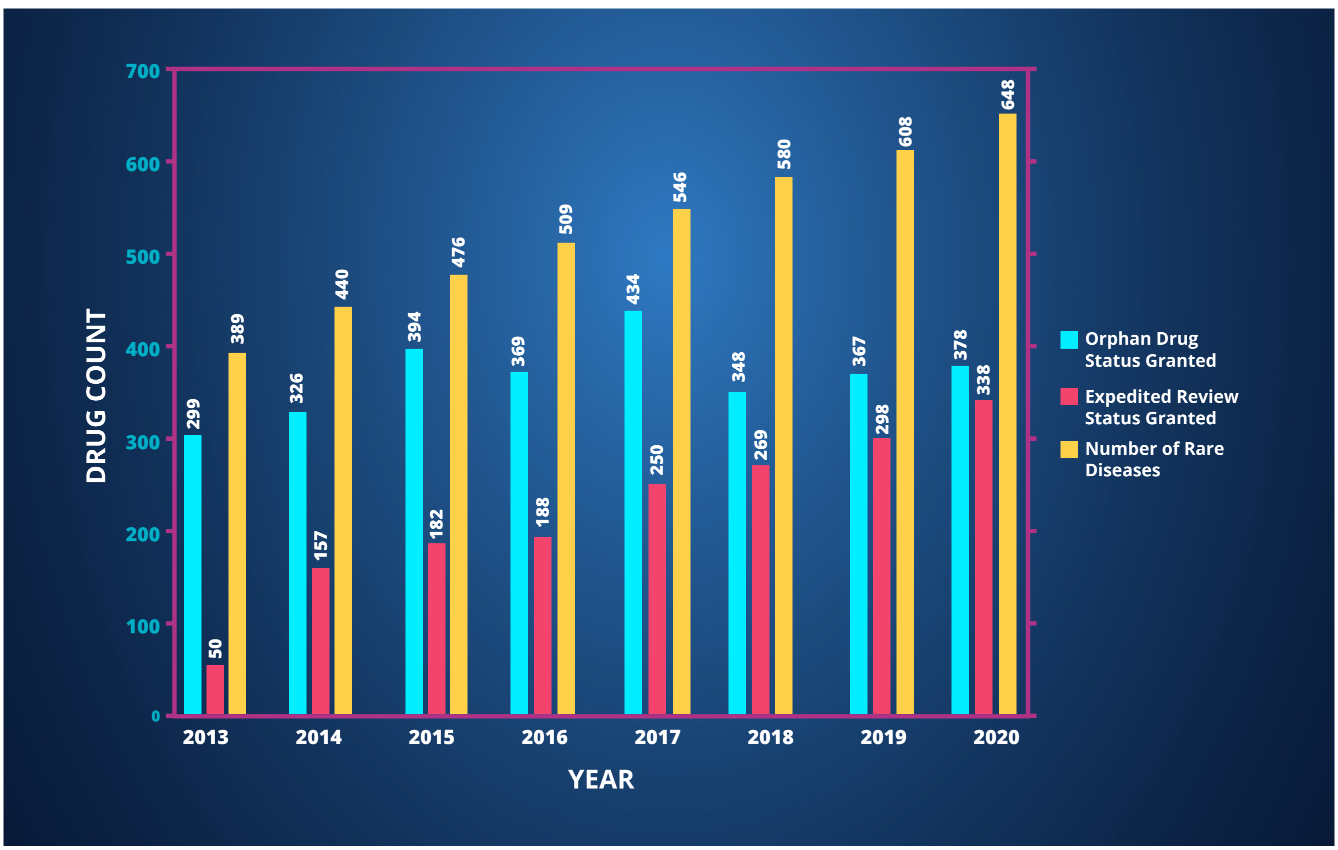
many in the industry. "The pandemic has revealed the inequities in our health care system and the vulnerabilities related to prioritizing preventive measures versus immediate therapeutics. These need equal attention to ensure both long-term and short-term solutions," noted Cameron Durrant, Chairman and CEO of Humanigen, quoted in *Scrip*.

Our sister service *Trialtrove* also has some dramatic data on the sheer volume of COVID trials which kicked off during 2020. The total number of trials involving treatments, vaccines or supportive therapies has now passed 4,000, with almost 2,000 currently under way and a further 1,600 planned. The US is again the top territory, with over 800 trials, but actually, region-wise, Asia comes out top with just over 1,200. By phase, the COVID trials break down as follows: Phase I – 488; Phase I/II – 248; Phase II – 1,696; Phase II/III – 340; Phase III – 828; Phase III/IV – 340; Phase IV – 351. Once again, all of this activity has appeared from nowhere little more than a year ago.

Taking a broader look at trials, anti-infective clinical studies are still like little shuttlecraft compared to the huge interstellar space cruiser which is oncology. Figure 15 shows that there are over 15,400 ongoing (open, closed or temporarily closed) trials in oncology at the moment, with a huge 6,500 at Phase II alone. CNS comes in second with around 5,400, beating infectious disease (4,700), which is in third place despite the COVID uplift.

Another favourite type of story for science fiction writers is that of an alternate reality or timeline. This concept has been exploited many times in books,

Figure 16: Rise in numbers of drugs receiving Orphan Drug status or an Expedited Review designation*, and the number of rare diseases under investigation, 2013–20



*Data for 2013 not complete as we only began systematically recording the dates of these events mid-year.

Source: Pharmaprojects®, January 2021

TV and movies, famous examples being the mirror universe visited in various iterations of the *Star Trek* franchise, and the 1990s series *Sliders*, whose whole concept was based around parallel universes. So, what might pharma R&D look like this year in an alternate timeline where COVID-19 had never existed? Maybe we have all been lost inside an *Inception*-like dream. But perhaps a better question might be, if we could jump in our souped-up DeLorean to go back in time and stop the outbreak happening, what would the pipeline look like when we got *Back to the Future*? Of course, it's impossible to say exactly how much COVID-19 has diverted resources away from other diseases, but our data in this section certainly suggest that a lot of the work here falls into the 'additional' category, rather than 'instead of'.

Finally in our chapter on therapeutics and diseases, we switch our attention to something COVID-19 is unfortunately not currently one of – rare diseases. The focus on one sadly extremely common disease hasn't dented the advance of research into rare diseases, with 5,608 different projects under development as of the start of 2021, up 6.1%, and thus outpacing pipeline growth as a whole. It is also a bigger numerical rise than seen in the previous year. [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)]. There are also more rare diseases being tackled than ever before. As Figure 16 shows, 648 rare conditions have drugs under development for them – up 40 from the previous year, which is the biggest increase since that seen in 2014. Meanwhile, the numbers of orphan drug and expedited review designations granted also rose to new record levels (both are associated with rare disease development).

> ***"The true delight is in the finding out rather than in the knowing."***
> - Isaac Asimov

Encounters of the Third Kind: Mechanisms and Targets

Pharma continues to go where no-one has gone before

Although science fiction is a broad church, covering speculative and dystopian fiction, time travel and invasions by monsters, probably its core subject in the minds of many is space travel and the discovery of new worlds. Unlike in science where there are no short-cuts, SF writers have come up with many ways to get their protagonists to bridge huge interstellar distances which, in reality, would take not just many lifetimes, but many millennia, to travel. *Doctor Who* has his or her TARDIS (which, handily, can go anywhere in time too), *Star Trek* its warp drive, the reboot of *Battlestar Galactica* its similar FTL jump drive, *Star Wars* travels via hyperspace, while *Interstellar* used black holes themselves. While these fantastical methods of travel sometimes permit our heroes to simply engage with their enemies, often the journey is based on something more altruistic – discovery. This is particularly true in the original *Star Trek* concept – famously described by its creator as 'a *Wagon Train* to the stars', with space as 'the final frontier'. The prime motivation for the *Enterprise's* voyages was 'to seek out new life and new civilizations' and to advance human knowledge via scientific discovery.

Similarly, the pharma industry's raison d'être must be to 'go where no-one has gone before', and discover new planets of drug mechanisms, and new species of drug targets. In this section, we will visit which mechanisms and targets are proving the most popular this year, and look at the level of discovery which is going on, as pharma pushes back the boundaries of its known universe.

The top 25 mechanisms of action, or pharmacologies, are listed in Table 5. 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. It's worth bearing that in mind while we look at the top 25.

Sitting atop the summit for a third year is one such general mechanism, immuno-oncology therapies. If anyone was in any doubt that COVID hasn't knocked cancer off its stride, they should consider the fact that the number of drugs for this broad strategy has grown by a further 10.6%, pulling further ahead of the even broader Immunostimulant class in second place (despite the fact that a lot of coronavirus vaccines would have been given this latter mechanism). The former is applied to all anticancer strategies where the therapy mobilizes the body's own immune system to identify and to attack its cancer cells, as opposed to drugs which act directly against a tumour. There is clearly an overwhelming faith in this strategy as a whole; to have almost 3,000 drugs in development, of which only 2.1% have as yet made it through clinical trials and into the registrational and commercial stages of development (represented by the development statuses pre-registration, registered and launched), is a phenomenal vote of confidence. It's certainly a rapidly evolving and complex field, which, as with much of immunology, is an incomprehensible as Klingon to anyone on the outside.

Table 5: Top 25 mechanisms of action (pharmacologies)

Position 2021 (2020)	Mechanism of action (pharmacology)	No of drugs 2021 (2020)	% of drugs PR/R/L	Trend
1 (1)	Immuno-oncology therapy	2,880 (2,605)	2.1	↑
2 (2)	Immunostimulant	1,410 (1,293)	10.6	↑
3 (3)	T cell stimulant	906 (718)	1.0	↑
4 (4)	Immune checkpoint inhibitor	432 (404)	4.4	↔
5 (7)	Gene expression inhibitor	191 (154)	2.1	↑
6 (6)	Angiogenesis inhibitor	190 (181)	23.2	↔
7 (5)	Immunosuppressant	181 (191)	39.2	↔
8 (8)	Radiopharmaceutical	174 (147)	9.2	↑
9 (11)	Genome editing	173 (117)	0.0	↑↑
10 (9)	Vascular endothelial growth factor (VEGF) receptor antagonist	142 (140)	19.7	↔
11 (14)	PD-L1 antagonist	125 (130)	4.0	↔
12 (10)	Apoptosis stimulant	114 (127)	14.9	↔
13 (30)	Natural killer cell stimulant	113 (64)	0.0	↑↑
14 (17)	PD-1 antagonist	113 (99)	10.6	↔
15 (13)	Immune checkpoint stimulant	109 (113)	0.0	↔
16 (21)	Microbiome modulator, live microorganisms	104 (85)	0.0	↑
17 (15)	CD3 agonist	100 (100)	1.0	↔
18 (18)	ErbB-2 antagonist	95 (97)	15.8	↔
19 (22)	Glucagon-like peptide 1 receptor agonist	91 (82)	9.9	↔
20 (16)	Cyclooxygenase 2 inhibitor	87 (100)	32.2	↓
21 (19)	DNA inhibitor	85 (96)	28.2	↔
22 (20)	Glucocorticoid agonist	76 (89)	50.0	↔
23 (12)	Opioid mu receptor agonist	75 (114)	40.0	↓
24 (24)	Cell wall synthesis inhibitor	73 (77)	38.4	↔
25 (23)	Tumour necrosis factor alpha antagonist	71 (76)	39.4	↔

Abbreviations used in table: PR = pre-registration; R = registered; L = launched

Source: Pharmaprojects®, January 2021

This table also provides ample evidence of the ongoing march of cell therapy approaches. The T cell stimulant category rises a remarkable 26.2% at number three, while the related natural killer cell stimulant category is our biggest chart climber, up from 30 to 13, which increases its pipeline size by an earth-shattering 76.6%. We'll return to this subject in the next section of the report.

In what is normally a chart which evolves only slowly, there is quite a degree of metamorphosis occurring this year. Appropriately enough, the Gene expression inhibitor category covering antisense and siRNA-type therapeutics climbs into the top five, while the Genome editing class enters the top 10 for the first time, with a 47.9% expansion rate. This latter category is applied to gene editing techniques such as CRISPR. It's one of a number of mechanism classes which make this year's top 25 despite having not one single drug which has moved beyond the clinical stages of development as yet. The use of live organisms to modify a patient's microbiome is another relatively new strategy which is gaining traction even though it's unproven. This strategy potentially has use beyond the obvious use in digestive disorders as we begin to understand more how the bacteria which always live inside of us affect the biochemistry of many different organs and tissues. These other species sharing our bodies are usually friendly and helpful if kept in the right balance, and are thankfully nothing like that most famous example of a gut-dwelling organism, the one which bursts out of John Hurt during that notorious scene in *Alien*.

Most of the other significant advances in the table are related to subclasses of the leading immuno-oncology class. At four is the second-level hierarchy term Immune checkpoint inhibitor, whereas outside of the top 10, mechanisms focusing on individual proteins involved in immuno-oncological techniques are really starting to make their presence felt, in the shape of the climbing PD-L1 antagonist and PD-1 antagonist categories. Bristol Myers Squibb is the leading exponent of drug development of this class, with 16 drugs. Some less household names come next: Innovent Biologics (10), Adze Biotechnology (nine) and Agenus (nine), with AstraZeneca completing the top five with eight.

A better way to examine the ecosystem of planet pharma is to look at the individual protein targets against which drugs are being designed. Table 6, which reports the leading 25 targets at the start of 2021, again highlights some of the year's notable trends. Her-2, an established target in primarily breast cancer, spends a second year at the top, now followed by another common cancer target, the epidermal growth factor receptor. The holder of the number one slot in 2019, the mu 1 opioid receptor, plummets this year from two to eight. Perhaps adverse publicity about the opioid addiction crisis, particularly in the US, has forced pharma into retreat on this front.

Elsewhere in the top 10, immuno-oncology makes its presence felt again in the other climbers. The CD3e molecule rises to number three with a significant 28.4% uptick. Its popularity reflects the fact that it is a target for BiTEs – bispecific T-cell engager antibodies. These agents consist of two single-chain variable fragments, one of which binds to T-cells via the CD3 receptor, and the other to a tumour cell via a tumour-specific molecule; thus, all drugs of this class have this target. Similarly, the majority of the drugs in the CAR-T cell therapy class use CD19 as a target, hence its continued march up the table to number four. Two other IO-related classes move up in overall numbers within the top 10: PD-L1 at number six, and PD-1 at seven.

Table 6: Top 25 drug protein targets

Position 2021 (2020)	Target	No of drugs 2021 (2020)	Trend
1 (1)	erb-b2 receptor tyrosine kinase 2 *[Her-2]*	163 (158)	↔
2 (3)	epidermal growth factor receptor	151 (148)	↔
3 (7)	CD3e molecule	149 (116)	↑
4 (5)	CD19 molecule	144 (121)	↑
5 (4)	vascular endothelial growth factor A	142 (143)	↔
6 (6)	CD274 molecule *[PD-L1]*	141 (116)	↑
7 (9)	programmed cell death 1 *[PD-1]*	122 (111)	↔
8 (2)	opioid receptor mu 1	112 (148)	↓
9 (8)	nuclear receptor subfamily 3 group C member 1 [glucocorticoid receptor]	100 (112)	↔
10 (15)	glucagon-like peptide 1 receptor *[GLP-1]*	98 (90)	↔
11 (13)	cannabinoid receptor 1	96 (97)	↔
12 (10)	prostaglandin-endoperoxide synthase 2 *[COX-2]*	96 (107)	↔
13 (11)	tumor necrosis factor	89 (101)	↓
14 (14)	opioid receptor kappa 1	84 (97)	↔
15 (16)	membrane spanning 4-domains A1	82 (78)	↔
16 (21)	TNF receptor superfamily member 17	76 (63)	↑
17 (12)	insulin receptor	72 (98)	↓
18 (17)	prostaglandin-endoperoxide synthase 1 *[COX-1]*	68 (76)	↔
19 (32)	TNF receptor superfamily member 9 *[CD137]*	68 (51)	↑
20 (-)	surface glycoprotein [severe acute respiratory syndrome coronavirus 2]	67 (-)	↑↑
21 (18)	dopamine receptor D2	66 (72)	↔
22 (19)	transient receptor potential cation channel subfamily V member 1	63 (69)	↔
23 (43)	5-hydroxytryptamine receptor 2A	60 (43)	↑
24 (25)	kinase insert domain receptor	58 (57)	↔
25 (23)	estrogen receptor 1	57 (60)	↔

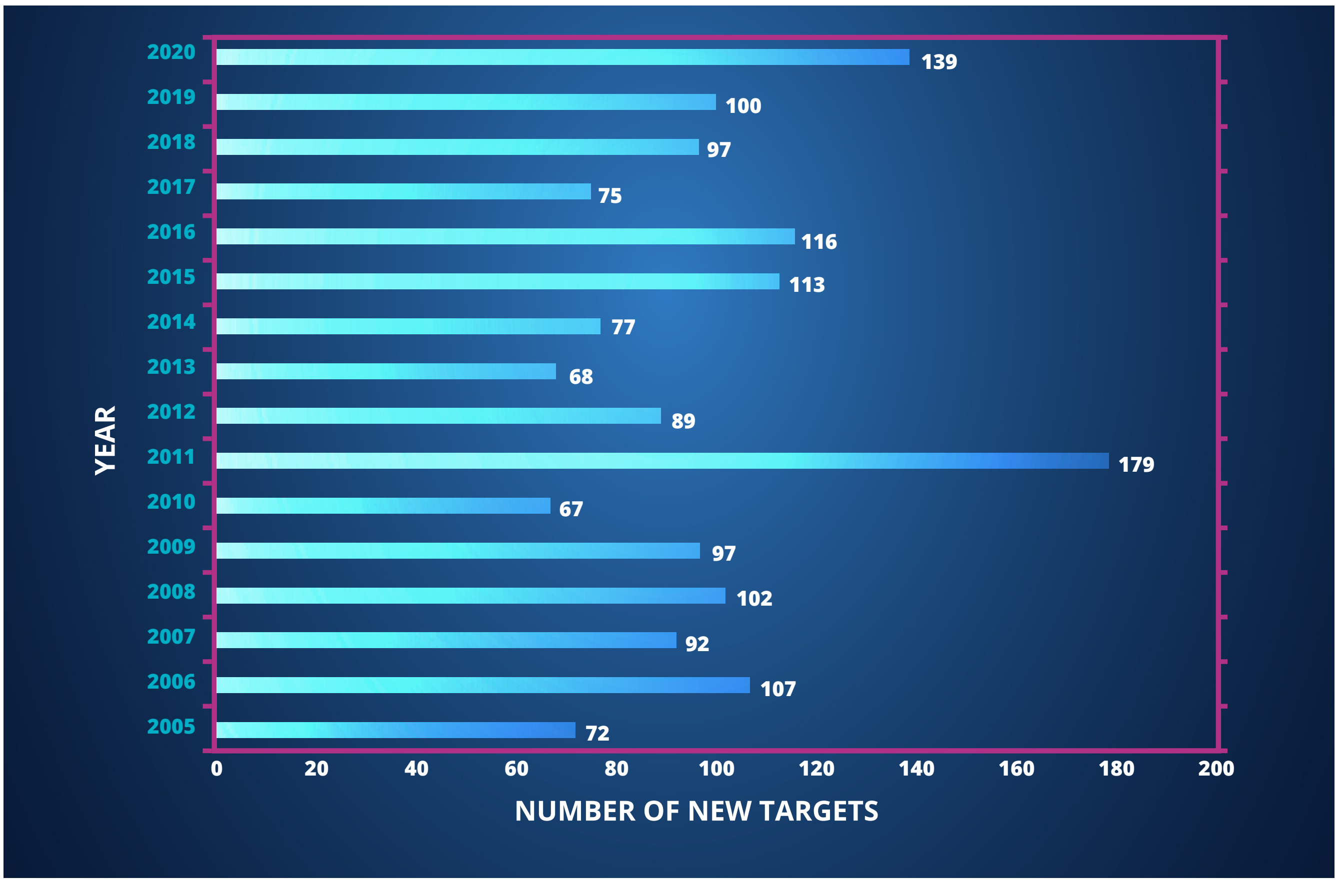
Note: NCBI names are used, except for additions in italics made by us for clarity.

Source: Pharmaprojects®, January 2021

Away from immuno-oncology, the glucagon-like peptide 1 receptor, a target pertaining primarily to type 2 diabetes and obesity, rebounds back into the top 10, while continued interest in cannabinoids is reflected just below. Conversely, insulins took a tumble. But there's no escaping the novel coronavirus, with a new entry at number 20 for the SARS-CoV-2 surface glycoprotein. More commonly known as the virus's spike protein, it forms the basis of many of the vaccine and monoclonal antibody strategies. It's also where we've seen mutations in many of the new variants which are causing concern at the start of the year. Whether we've seen sufficient mutations in this protein to escape current vaccines is a matter of conjecture as I write, although the companies involved seem confident that they can tweak their vaccines relatively quickly if needed. It's likely that the virus versus vaccine struggle will be an ongoing battle for some years to come, just as it is with influenza and today's flu vaccines.

The other new entries into this year's chart are CD137 at number 19, a co-stimulatory immune checkpoint molecule; and the return of the 5-HT2A receptor at number 23. The latter is an established target for a number of neuropsychiatric diseases but was buoyed last year by an unusually large number of new drugs entering the database which hit it, although many of these were reformulations of existing drugs rather than a raft of new ones. Exiting the scene this year were the HIV gag-pol protein, the β2 adrenoceptor and solute carrier family 6 member 2. The departure of the HIV target from the top 25 demonstrates how quickly a global pandemic can seem like just a wrinkle in time once pharma gets to grips with it.

Figure 17: Number of new drug protein targets identified by Pharmaprojects, by year



Source: Pharmaprojects®, January 2021

Comparing this table with its equivalent from a decade back would certainly confirm the fact that the pharmaceutical industry has done a great job in venturing to hitherto unexplored corners of the drug universe. But what about the real cutting-edge stuff so new it's almost in a different dimension, how good was the industry at doing that over the past 12 months? Figure 17 would suggest that despite all of the restrictions on all of our working practices, science marched on, and actually 2020 was an excellent year for innovation. Targets for which drugs were identified for the very first time numbered 139, making it the second-best year since records began in 2005. In this regard, it was only beaten by 2011, where an anomalously high figure was recorded as bacterial targets were added to the *Gene* database. This is an excellent result for the industry. The total number of targets currently being hit by drugs in active development also rose, standing now at 1,858, up from last year's 1,766. This should provide a great launchpad for further stellar successes though the 2020s.

> ***"In science fiction, we dream. In order to colonize in space, to rebuild our cities, which are so far out of whack, to tackle any number of problems, we must imagine the future, including the new technologies that are required"***
>
> \- Ray Bradbury

The Fourth Dimension: Types of Pipeline Drugs

The Force is with biologicals

Our final set of analyses focus on the different kinds of drugs in development and their delivery. Much like science fiction aliens, drugs can come in many shapes or forms. For many years, the pharma scene was almost exclusively populated by different kinds of small molecules, pretty much all based on the same technology, in the same way that many alien races in TV shows tend to be variations-on-a-theme humanoids (*Star Trek* famously has lots of variations on races with different kinds of bumpy foreheads). Since the rise of biotechnology from the 1960s and 1970s, though, new kinds of therapeutic beings have emerged. Perhaps biotech drugs could be considered as pharma's cyborgs – precisely constructed from new technologies to perform certain highly specific tasks. So, are the machines taking over?

Table 7 breaks the current pipeline down by the origins of each drug, based on *Pharmaprojects*' 'origin of material' classification. As with the mechanisms of action classification, there is hierarchy here: thus, Biological protein, antibody and Biological protein, recombinant are subclasses of Biological, protein, with the latter term only being applied if a more specific subclass is not known. This classification also doesn't have an 'Unknown' category, with drugs for which their type is not reported or disclosed being assigned to the general Chemical, synthetic class as a default. As a result, some of the drugs in the category at the number one position may subsequently be recast into other roles once more information comes to light. Nonetheless, the vast majority of its 9,000+ constituents will be drugs in the general class of small molecules produced via traditional synthetic chemistry techniques.

The more machine-tooled monoclonal antibodies are indeed advancing on their rivals, though. At number two in the table, MAbs posted an 11.7% rise, again fuelled in part by a raft of new antibody therapies under development for the treatment and prevention of COVID-19. The disease is also behind a big increase seen in nucleic acid-based therapies, and in biologicals delivered via virus particles (for example, the AstraZeneca/Oxford Biomedica COVID vaccine). The novel coronavirus is like an alien which has its monstrous tentacles everywhere.

Heterologous cellular therapies, where cells are taken from one source and introduced into the patient, also make a *Fantastic Voyage* up our table, presenting the largest increase of all, both numerically (+146) and percentage-wise (+48.3%). Higher up, autologous cell therapy (cell therapy using the patient's own cells) posts a more modest but still significant 25% expansion in pipeline size.

How far are the androids of biotech advancing? Figure 18 shows that the percentage of the pipeline which can be ascribed a biotech origin is up once more, and is now at 42.9%, up a further 2.5% from the 2020 value. The revolution has been under way gradually for over 20 years now, and it seems likely that if the march of the machines continues at this rate, biotechnology-based drugs could become the dominant lifeforms in the pharma biosphere before the end of the decade.

Table 7: Top 25 origins of pipeline drugs

Position 2021 (2020)	vTarget	No of drugs 2021 (2020)	Trend
1 (1)	Chemical, synthetic	9,007 (8,921)	↔
2 (2)	Biological, protein, antibody	2,484 (2,224)	↑
3 (3)	Biological, protein, recombinant	771 (795)	↔
4 (4)	Biological, cellular, autologous	758 (602)	↑
5 (6)	Biological, nucleic acid, viral vector	563 (549)	↔
6 (5)	Biological, protein	562 (485)	↑
7 (7)	Chemical, synthetic, peptide	475 (478)	↔
8 (8)	Biological, cellular	459 (464)	↔
9 (9)	Biological, virus particles	458 (405)	↑
10 (12)	Biological, cellular, heterologous	448 (302)	↑↑
11 (10)	Chemical, synthetic, nucleic acid	437 (401)	↑
12 (16)	Biological, nucleic acid	296 (205)	↑↑
13 (11)	Natural product, plant	260 (306)	↓
14 (13)	Biological, peptide	259 (257)	↔
15 (15)	Biological, bacterial cells	251 (218)	↑
16 (14)	Biological	224 (245)	↓
17 (18)	Biological, other	155 (132)	↑
18 (17)	Biological, peptide, recombinant	141 (147)	↔
19 (19)	Biological, nucleic acid, non-viral vector	136 (127)	↔
20 (20)	Chemical, semisynthetic	57 (61)	↔
21 (21)	Natural product, bacterial	54 (60)	↔
22 (22)	Natural product	39 (49)	↓
23 (24)	Natural product, fungal	39 (29)	↑
24 (23)	Natural product, animal	31 (29)	↔
25 (25)	Chemical, synthetic, isomeric	21 (21)	↔

Source: Pharmaprojects®, January 2021

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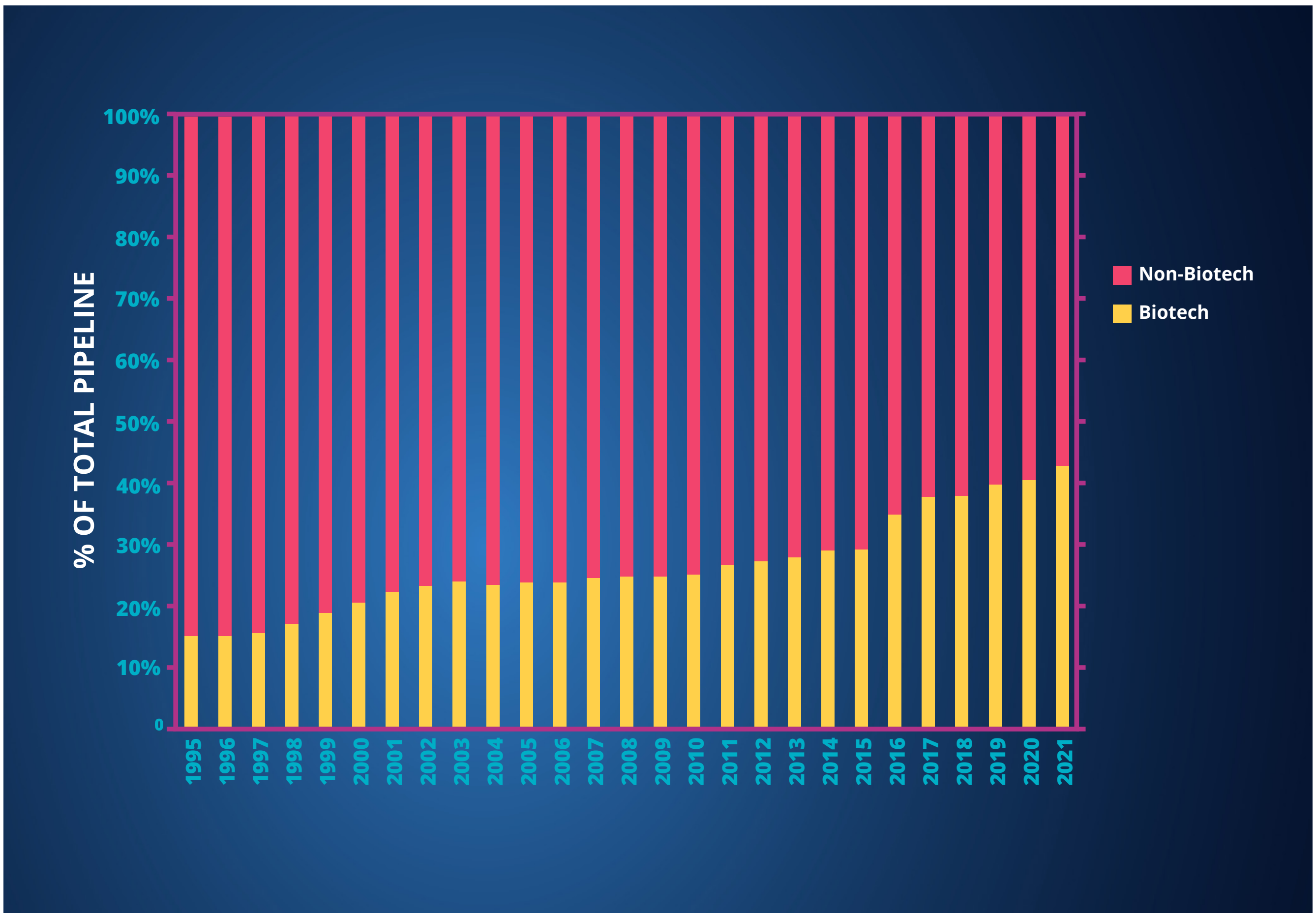
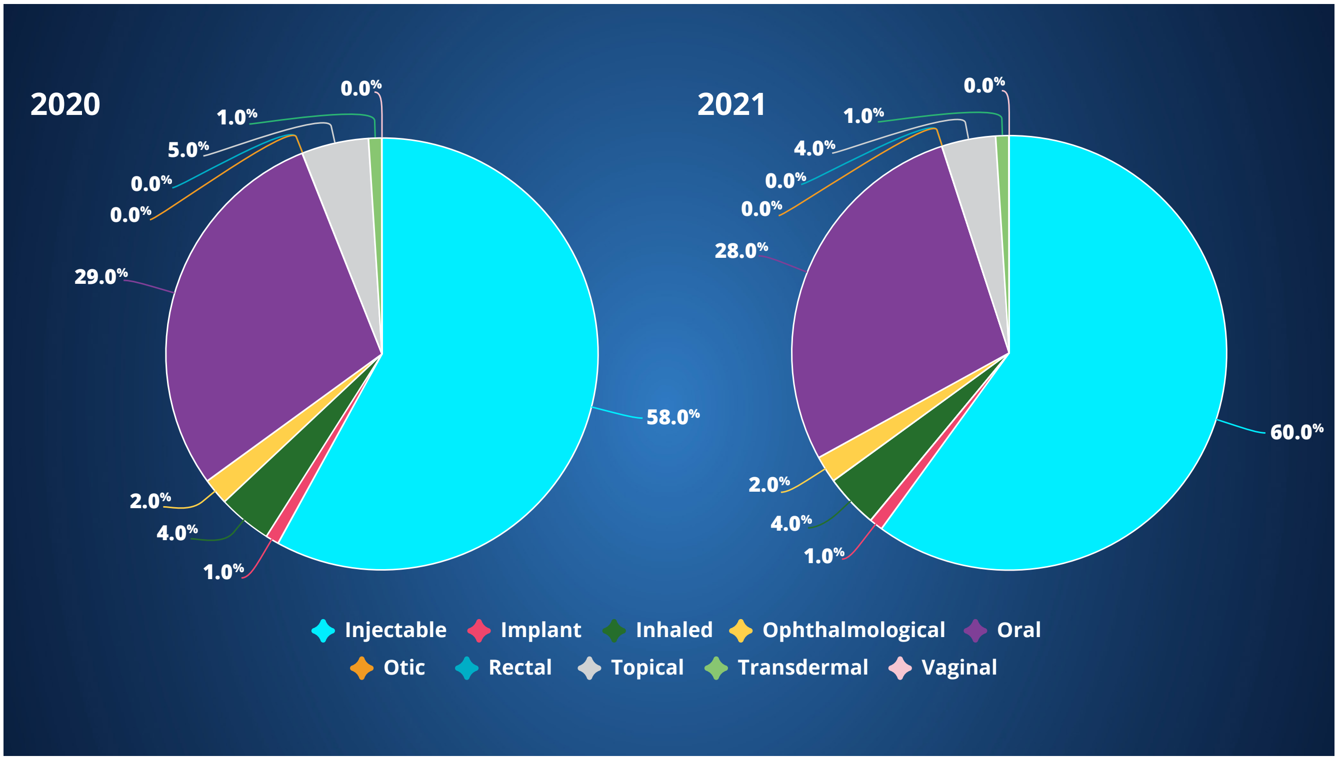
The ongoing migration to biotech has again had a concomitant effect on the way in which drugs are delivered. Figure 19 shows that the proportion of pipeline drugs delivered by injection has risen from 58% to 60%, which is counterbalanced by 1% falls for both oral and topical agents.

Figure 18: Biological versus non-biological drugs as a percentage of the pipeline, 1995–2021



Source: Pharmaprojects®, January 2021

Figure 19: Pipeline by delivery route, 2020 and 2021



Source: Pharmaprojects®, January 2021

"It is good to have an end to journey toward, but it is the journey that matters in the end."

- Ursula K Le Guin, The Left Hand of Darkness

To Infinity and Beyond: Escaping the Black Hole

As we reach the end of our 2021 report, how can we sum up 2020? At times, it felt like we were in a spaceship attempting to break free from disaster and destruction which the black hole of COVID is attempting to suck us towards. Every time we appear to have passed beyond the event horizon, the pandemic's pull strengthens and renews its malign influence on us. At the time of writing in January 2021, we are being buffeted by further gravitational waves of new strains which seem to be more infectious and might be more deadly. We thought this would all be over by June, and then by Christmas, yet here we are, in a third lockdown in the UK, and with fatalities surging past the grim 100,000 milestone, whereas in the US, the half a million mark is not far off. Will 2021 be the year we begin finally to pull clear?

Certainly, the frankly phenomenal success in bringing vaccines to the market so rapidly looks like giving us the booster thrust we so badly need. It is almost as if those vaccines were developed via some kind of time dilation or variation of the twin paradox, the famous thought experiment in special relativity explored in many science fiction works such as Robert A Heinlein's *Time for the Stars*, Orson Scott Card's *Ender's Game* and Christopher Nolan's film *Interstellar*. It's as if Pfizer, Moderna, AstraZeneca and the like blasted off into space to do their vaccine R&D at speeds close to that of light, returning after 10 years of vaccine development to find that on Earth, only 10 months had passed. It's a fantastic achievement, and one which looks like, to paraphrase the opening credits of SF TV show *Babylon 5*, "our last, best hope for peace" in the war against the evil alien COVID.

Fortunately, it looks like we haven't quite needed to divert all power to the warp engines at the expense of shutting down life support to other parts of the good ship pharma. While there were inevitable delays to clinical trials during the first wave of the pandemic, the industry has now had time to adapt and learn to do things in new ways. Overall, there doesn't seem to be much evidence of COVID sucking the life, *Alien*-like, out of other bodies of work. Let's not forget that the total number of drugs in R&D is at record levels this year, with any stunting of the existing pipeline more than offset by a whole new COVID-related market opening up. And we've seen that the industry was unusually agile in mobilizing its *Starship Troopers* to an unprecedented degree during the first few months of the crisis.

It's impossible to get an accurate view on how different the pharma R&D pipeline might look in 2021 had COVID-19 not come along. But would we want to clamber into *Doctor Who's* TARDIS or HG Wells' *Time Machine* and go back in time and change the single event which led to the global outbreak (whatever that was)? Time travel itself is of course another rich seam for science fiction writers, especially going back in time to change the past, and the risks in doing so. The most extreme example is the so-called 'grandfather paradox', whereby a person goes back in time and kills their grandfather before their father has been conceived, thus preventing their own existence and ability to carry out the act. This feature, and variations thereof, is covered in the *Back to the Future* trilogy and other notable SF film hits such as *12 Monkeys* and *The Terminator*. Or there is the butterfly effect, whereby even a tiny change wrought by the time traveller can have huge unforeseen consequences (see Ray Bradbury's short story *A Sound of Thunder*, from where this term originated).

Well obviously we don't have the option to go back and prevent the SARS-CoV-2 outbreak and save the millions of lives it has sadly taken. But if we did, what positive things might we have eliminated too? The most palpable of these is the turbocharge which vaccine R&D has received. While companies such as Moderna and BioNTech had been working on the technologies which they used in their COVID vaccines for a number of years, they could not have expected the shot in the arm, if you pardon the pun, which the pandemic afforded their businesses. I think it's fair to say that we will be benefitting from the stimulus which vaccine research has received for many years to come. Much as the Second World War fast-tracked rocket technology research and led to the moon landings, great leaps forward can come out of the ashes of truly terrible world events.

Another big positive which pharma can take from the experience of the past 12 months is the enhanced collaboration we've seen across the industry. At the time of writing, both Sanofi and Novartis have just announced that they are stepping in to help their erstwhile rival Pfizer and will assist with the production of doses of the latter's COVID-19 vaccine in Europe. This will inevitably be at the expense of the companies' own manufacturing capacities, and is something which would have been almost unheard of a year ago. It's just one of numerous examples where companies have put aside their usual business rivalries to work together for the greater good. In the past 12 months, to paraphrase a famous quote from sci-fi classic *Blade Runner*, "We've seen things you people wouldn't believe." The question is whether this will be sustained when things go back to 'normal' – whatever that is.

And the pharma industry has undeniably learnt a lot in how to do things differently in 2020. It should be commended for not losing the plot (unlike last year's most confusing SF movie, *Tenet*) or going into stasis. New ways to conduct research and, in particular, run clinical trials had to be rapidly put into place. Many of these innovations will benefit the industry in terms of improved efficiency, and trial participants in terms of improved convenience, for years to come. Plus, pharma continues to make huge strides in the areas which were its key focus before all this happened, like cancer and in particular immuno-oncology, and in rare disease R&D.

Finally, it's likely that the pharmaceutical industry will take a sizeable reputational enhancement from the events of 2020, and indeed 2021. Pharma has long been bashed in the lay press for its high drug prices, for its slowness, and even for the temerity it has to insist on making a profit. But having stepped up during the coronavirus crisis, we can all see clearly what benefit it can bring to humanity once it puts its mind to it. Going into this new year with record levels of infections and deaths but not having vaccines already rolling out simply doesn't bear thinking about. The pharma industry really has ridden to all of our rescues and is beaming us up out of danger.

So, as we begin to escape the intense gravitational pull of the dark star of COVID-19, and re-engage with the universe as a whole, the industry can take all of the above positives forward. How will pharma fare during the recovery and return phase? Many industry commentators are bullish, excited even. Quoted in *Scrip* (https://scrip.pharmaintelligence.informa.com/SC143662/Scrip-AsksWhat-Does-2021-Hold-For-Biopharma-Part-2-COVID-19-Shock-Waves-And-Silver-Linings#R&D), Mahesh Karande, President and CEO of Omega Therapeutics, noted that, "In 2020, biopharma has come through not only as a saviour in the pandemic by creation of life-saving vaccines, but also as a bright spot in the economy where people have continued to find employment and growth. This dual status will continue in 2021. We will see newer and bolder approaches to biology and continued tackling of previously undruggable targets and diseases. 2021 will go down as one of the golden years of biopharma." In the same article, another top pharma exec, Tmunity Therapeutics' President and CEO Usman 'Oz' Azam, sounded similarly exhilarated: "2021 will be a transformative year for biopharma and the life sciences," he said. "It will be the year where the credibility and power of science applied to human health will shine. It's the year that we will hopefully recognize the personal investment by countless women and men in the life sciences around the world that tirelessly helped to stem a modern pandemic by developing innovation at breakneck speed. It's the year where we will dare to say we can see a path to 'cure' certain diseases. It's the year we will realize hope after the dark."

Science fiction is a genre which can hold a mirror up to our lives, but it's one in which there isn't always a happy ending. Books and movies are littered with dystopian codas where everybody dies, the aliens take over, or the world, or even the universe, ends. 2020 was certainly a year with a whole *Avengers*-style franchise's worth of incident – and I didn't even mention the demise of the Donald, or Brexit.

It was a year of loss, of anxiety, of fear. But thanks in part to its adaptability, resilience, creativity and the giant pulsating brains of those who work in it, pharmaceutical R&D looks set to teleport us into a *Brave New World*, with COVID exterminated, and with a stronger and more technologically advanced industry than ever before. Maybe this is a story where the *Alien* gets flung out through the airlock, humanity ascends to a higher plane of existence at the end of its *Space Odyssey*, and *E.T.* gets to phone home. However things pan out, *Pharmaprojects* will be in the cinema, taking notes and casting a critical eye, so next year, like *The Terminator*, 'I'll be back'. But to quote the famous Vulcan greeting from *Star Trek*, with a successful pharma industry pushing back the boundaries of science, it is to be hoped that we can all 'Live long and prosper'.

"The future is not Google-able"
- William Gibson

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 analyzing trends in pharma R&D. For over 25 years, he has authored the "Pharma Annual R&D review" and its new active substances (NAS) launches supplement. This has become a must-have industry report for those seeking to identify the changing fortunes of drug R&D. Ian joined Pharmaprojects in 1987, when it was part of PJB Publications. It was acquired by Informa in 2003. He previously worked in molecular biology as a research assistant at the University of Bristol.

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Accurate and timely intelligence about the drug development pipeline is vital to understanding the opportunities and risks in today's biopharmaceutical marketplace—whether you are targeting an unmet medical need, investigating promising new therapies or researching drug development historical trends and treatment patterns. If you are providing contract research or other services in the pharma industry, you need to stand out. A solid understanding of your potential clients' pipelines and competition will help you leave a lasting impression.

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