Citeline

Informa Pharma Intelligence

2021 Completed Trials: Green Shoots of COVID-19 Recovery Become Apparent

WHITEPAPER

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Introduction

As the COVID-19 pandemic stretched through a second year, its impacts continued to reshape the clinical trials landscape. Trialtrove recorded 4,109 industry-sponsored clinical trials from Phase I through to Phase III/IV that either reached completed status or reported primary endpoints during 2021.[1] This number exceeds the tally of 3,777 in 2020 and represents an 8.8% annual increase, which is double the growth rates observed in the pre-pandemic period from 2017 through 2019 (3.0–4.3%). An additional 838 studies reported terminations in 2021, which is a 21% decrease compared with those reporting termination in 2020 (1,067). Both of these directional changes point towards the early signs of a recovery from the disruption caused to ongoing clinical trials in 2020.

The Oncology, Infectious Diseases, and Vaccines therapeutic areas all saw substantial growth, while the remainder either grew modestly (Autoimmune/Inflammation, Central Nervous System, Ophthalmology) or decreased their trial completions (Metabolic/Endocrinology, Cardiovascular, Genitourinary). A massive increase in COVID-19 trial completions was the major driver to overall trends and the observed 8.8% topline growth. However, this disease area also was uniquely impacted by high trial terminations, due to challenges in recruitment and logistical factors.

Despite the turbulence caused by COVID-19, the leading clinical trial sponsors achieved success rates comparable to those in 2019 in trials conducted across a wide array of rare and prevalent diseases. This top 20 group of companies continues to focus on global trials, although the increased domestic trial activity by Chinese sponsors is now making a mark on overall completed trial trends. Within the top three therapeutic areas of Oncology, Infectious Diseases, and Autoimmune/Inflammation, the current trends and major players are further explored in this white paper.

1. The snapshot of clinical trials completed between January 1, 2021 and December 31, 2021 was taken on February 14, 2022. Industry sponsors are classified as "Industry, Top 20 pharma" or "Industry, all other pharma".

Topline Trial Landscape Metrics

Oncology continued to place at the top spot among rankings of therapeutic areas (TAs) for completed trial activity in 2021. For the first time, Infectious Diseases (ID) was catapulted from fifth into second place owing to considerable COVID-19 pandemic-related trial activity. The Autoimmune/Inflammation (A/I) TA attained third rank, while Central Nervous System (CNS) and Metabolic/Endocrinology (Met/Endo) dropped into fourth and fifth places, respectively. Cardiovascular (CV) continued its decline in completed trials observed since 2018. Vaccines, which often overlaps with ID trials, retained its seventh place while completing substantially more trials in the past year. The smallest TAs, Ophthalmology and Genitourinary (GU), are trending in opposite directions with modest changes in their trial counts.

Table 1. Trial counts and rankings for completed trials, by year

Therapeutic area	Ranking				Trial Count[a]			
	2021	2020	2019	2018	2021	2020	2019	2018
Oncology	1	1	1	1	1,222	1,128	1,124	1,073
Infectious Diseases[b]	2	5	5	5	726	485	449	481
Autoimmune/Inflammation	3	2	3	2	700	665	775	713
CNS	4	3	2	3	620	617	787	677
Metabolic/Endocrinology	5	4	4	4	545	567	675	607
Cardiovascular	6	6	6	6	303	308	316	360
Vaccines	7	7	7	7	231	157	175	166
Ophthalmology	8	8	8	8	97	92	94	80
Genitourinary	9	9	9	9	62	66	79	79

[a] Trials may span multiple therapeutic areas.

[b] Excludes Vaccines trials.

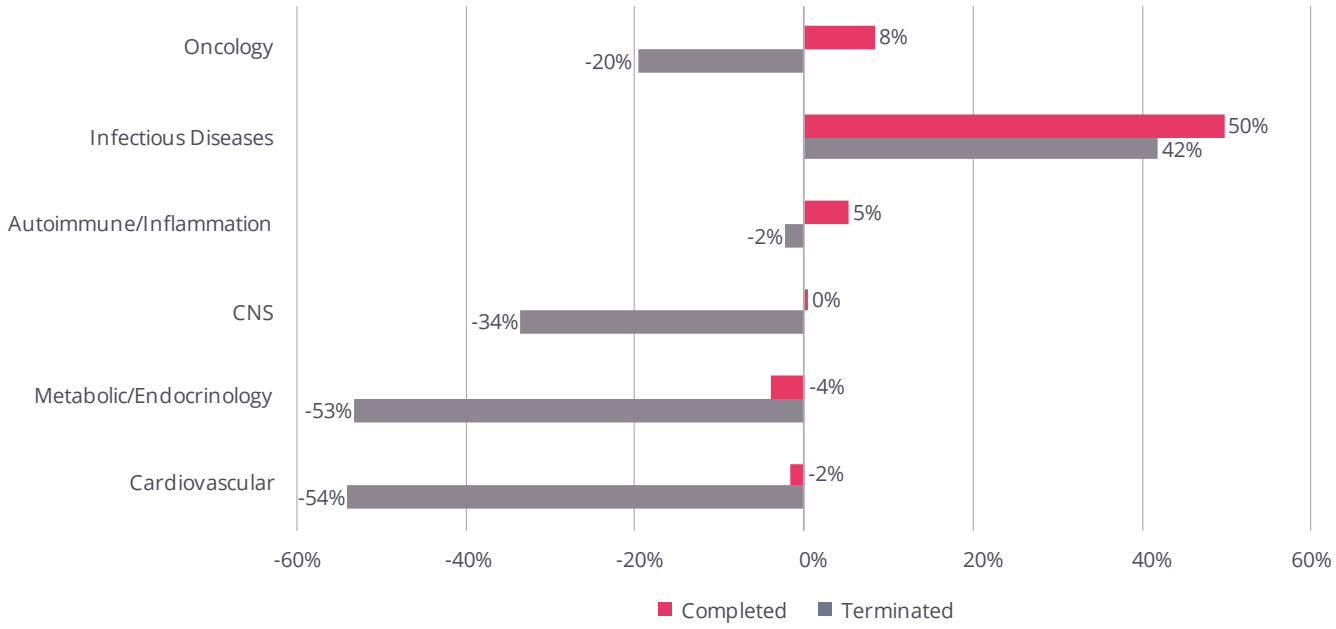
Source: Trialtrove®, February 2022

COVID-19 pandemic impacts on trial completions and terminations

Multiple factors collectively determine the annual trends observed for each TA. These factors include the counts of completed and terminated trials, plus the timelines of ongoing trials whose progress may have been affected by the pandemic. The analysis of relative changes in both completed and terminated trial counts revealed interesting changes and TA-specific differences compared with last year's trends (Figure 1).

Notable increases in completed trials were observed in ID (49.7%), Vaccines (47.1%), and Oncology (8.3%). Both ID and Vaccines also saw the highest increases in termination rates, with year-on-year changes of 42% and 111%, respectively. It should be noted that despite this high percentage change in Vaccines, the absolute numbers remain low with only 19 trials terminated, compared with nine in 2020, and these trials also are classified in the ID TA as COVID-19 studies. In A/I, trial completions increased by 5.3% while terminations decreased modestly (-2%; 137 versus 140). Terminations also decreased, year-over-year, for Met/Endo (-53%; 57 versus 122), CV (-54%; 39 versus 85), and CNS (-34%; 89 versus 134). Their completed trial counts changed modestly, with declines in Met/Endo (-3.9%) and CV (-1.6%), while CNS remains essentially flat (0.5%) after a period of growth observed in 2018 and 2019. The numbers of completed trials in the smallest TAs, Ophthalmology and GU, are shown in Table 1. Ophthalmology and GU each recorded 13 terminated trials in 2021, which is an increase compared with their 2020 counts of seven and four trials, respectively.

Figure 1. Relative change in 2021 for completed and terminated trials, by therapeutic area

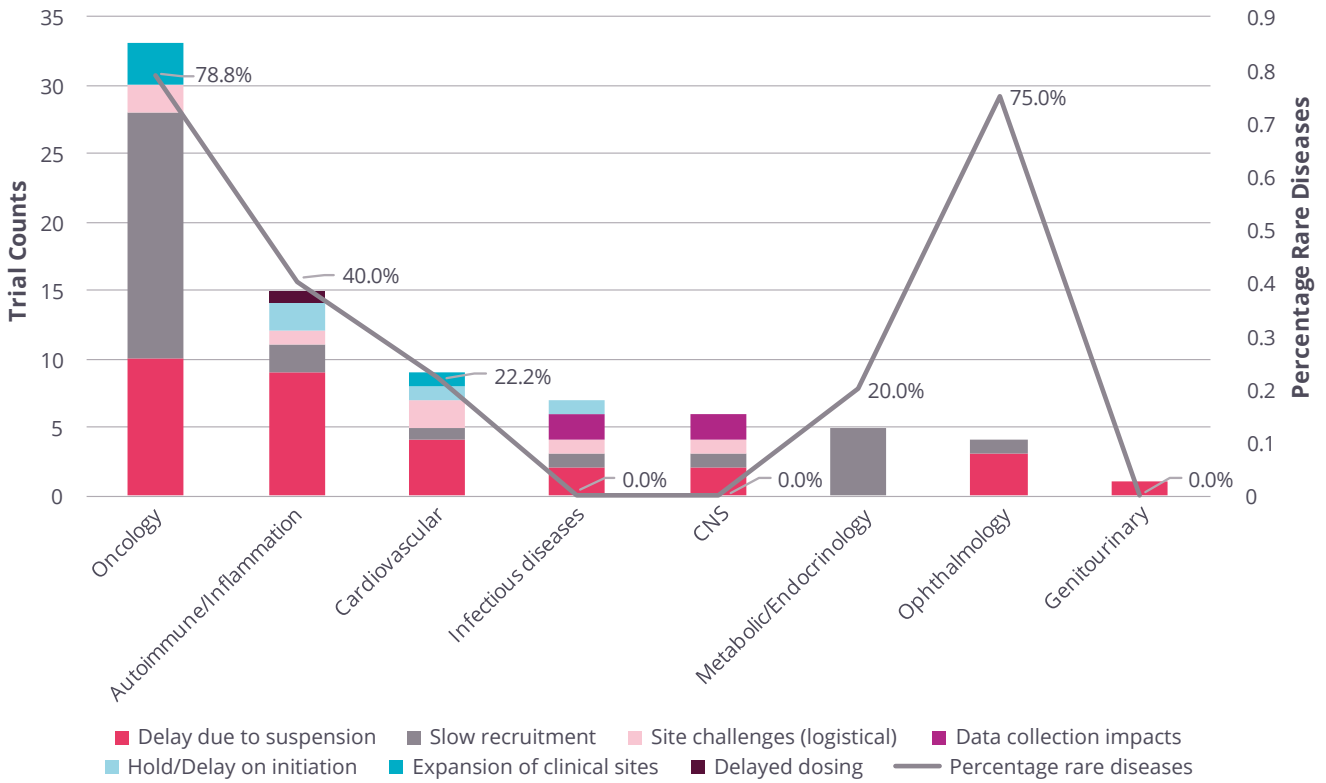


Source: Trialtrove®, February 2022

In the last annual edition of this white paper, it was demonstrated that various COVID-19 related impacts extended the timelines for ongoing/planned studies that had projected a primary completion date in 2020.[2] To determine whether sponsor-disclosed COVID-19 related reasons for

delays had changed in 2021, this analysis was repeated with a focus on TA-specific trends and rare diseases (Figure 2). The total number of delayed trials increased annually from 52 to 78, while the major reasons for delays remain the same: delay due to suspension (31 versus 22) and slow recruitment (29 versus 19). Delayed oncology trials increased most dramatically, from to 13 to 33 trials, and were mainly due to suspensions and slow recruitment. Trials enrolling patients with rare diseases often enroll slowly under normal circumstances and could be further delayed during pandemic conditions. A filter for rare diseases reveals that suspensions and slow recruitment are the most prominent reasons in TAs with the highest rare disease percentages. Oncology includes many rare diseases, accounting for 78.8% of its delayed trials. The rare indications in A/I are scleroderma, pulmonary fibrosis, cystic fibrosis, and infant respiratory distress syndrome, and these comprise 40.0% of the delayed trials. In Met/Endo, there is a single rare disease trial for adrenal insufficiency (20.0% of five delayed trials). There are two rare disease trials in CV for severe hypertension (22.4%) and three in Ophthalmology (75%) for retinitis pigmentosa. The ID and CNS TAs included no rare disease trials and were delayed for a wider range of reasons, beyond recruitment delays.

Figure 2. COVID-19 impacts in ongoing or planned trials, projected to have completed in 2021, by therapeutic area and percentage of rare disease trials



Source: Trialtrove®, February 2022

2. Informa Pharma Intelligence (2021) 2020 Completed Clinical Trials. Available from: https://pharmaintelligence.informa.com/~/media/informa-shop-window/pharma/2021/files/whitepaper/completed-trials-2020-whitepaper.pdf [Accessed April 4, 2022].

Finally, we consider trial terminations reported in 2021, which were substantially fewer in all TAs except for ID and Vaccines. The majority (64.3%) of terminated ID trials were COVID-19 treatment or vaccine studies (Table 2). The major reasons reported for termination were poor enrollment and logistical challenges (often tagged with the reason Other); for example, insufficient operational capacity or study personnel, and reduced community spread of influenza. The other TAs also experienced business- and pandemic-related terminations in the past year, but their termination levels declined compared with 2020. This suggests that for conventional areas of clinical research, 2021 has seen a return to normality compared to the disruptions caused in 2020.

Table 2. Terminated infectious disease trials, by termination reasons

Disease	Poor enroll-ment	Other	Lack of efficacy	Business decision – Other	Business decision – Pipeline reprioriti-zation	Business decision – Drug strategy shift	Lack of funding	Safety/ adverse effects	Total
Infectious diseases (total)	37	36	18	16	9	5	4	4	129
Novel coronavirus (2019-nCoV, COVID-19)	29	22	15	9	5	3	0	0	83

Trials may span multiple ID diseases, and include COVID-19 trials.

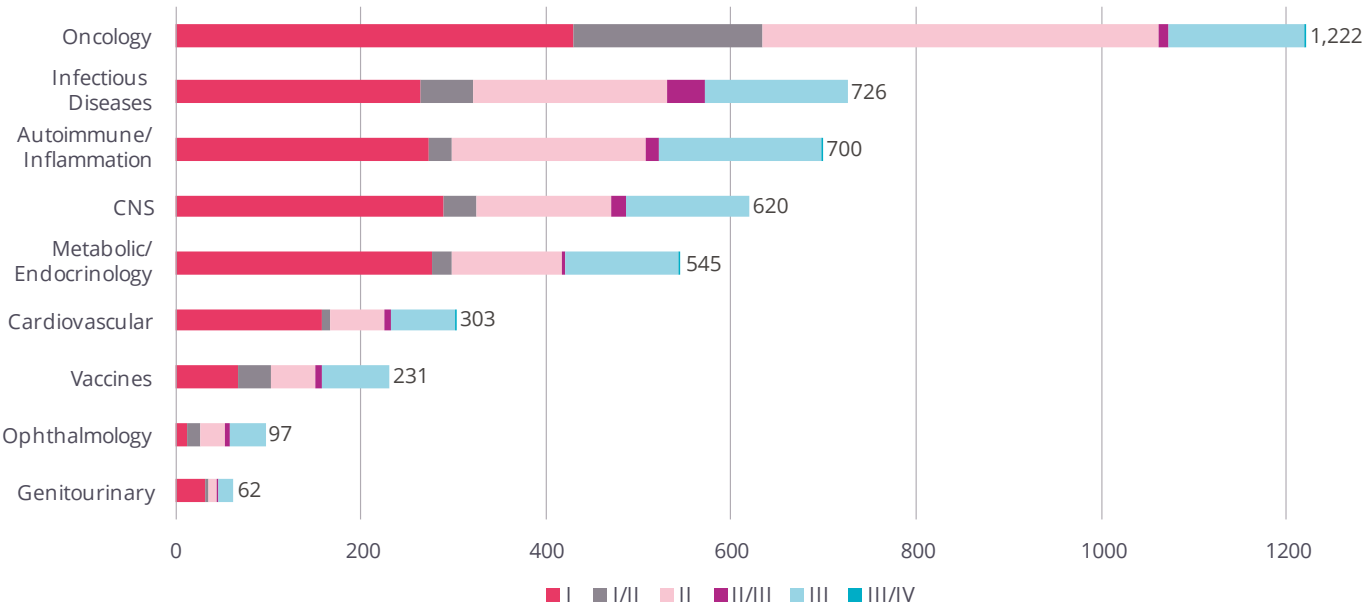
Source: Trialtrove®, February 2022

Distribution of 2021 completed trials by therapeutic area and phase

The expected distribution of trial counts by phase was observed again this year, with fewer later-phase trials completing than those of earlier phases for most TAs. Historically, Oncology completes a two-fold lower proportion of Phase III trials (~12–13% for the past three years) than other TAs (~21–25% for A/I and CV). Oncology's profile is similar in 2021, including nearly identical Phase I and Phase III trial counts, indicating that the growth in Oncology can be traced to increased Phase I/II and Phase II activity (~15.8% each). The dramatic jump in completed ID trials (49.7%) comprised of roughly proportional increases across all phases. The profiles for the mid-sized TAs include annual increases in Phase I trials (A/I, 30.5%; CNS, 11.1%; Met/Endo, 10.4%; CV, 16.3%), and decreases in both Phase II (A/I, -8.7%; CNS, -8.2%; Met/Endo, -5.5%; CV, -22.4%) and Phase III (A/I, -10.7%; CNS, -11.3%; Met/Endo, -18.0%; CV, -13.6%) completions.

This trend towards growth in earlier phases of research and reductions in larger clinical trial completions indicates that the pandemic recovery is still ongoing, with the multi-year timelines of Phase III trials in particular more prone to disruption. The 2021 counts were also augmented by increased activity captured from Chinese registries. These trials generally are run exclusively in China.[3] Most of these trials, ranging from 67.5% to 82.1% for mid-sized TAs and 55.0% for Oncology, are Phase I or Phase I/II studies (data not shown), a factor that accounts for most of the growth in that phase observed during this period.

Figure 3. Distribution of industry-sponsored trials completed in 2021, by therapy area and phase



Source: Trialtrove®, February 2022

3. Pharma Intelligence (2021) China Clinical Trials Landscape. Available from: https://pharmaintelligence.informa.com/resources/product-content/introduction-to-the-china-clinical-trials-landscape-with-andy-benson [Accessed March 24, 2022].

The top five diseases for trial completions in 2021 (Table 3) were COVID-19, non-small cell lung cancer (NSCLC), respiratory infections, breast cancer, and type 2 diabetes (T2D). The global COVID-19 pandemic is being met with vigorous research and development by the industry. COVID-19 trials reached a new high for an individual disease (354), having tripled its count since 2020 (116) and attaining the top place. The top Oncology disease, NSCLC, is ranked second, and its count has continued to grow since 2018. By contrast, T2D and breast cancer have dropped, both in rank and trial counts, during the same period. Respiratory infections completions have increased modestly over the past four years, and it occupies the third place again this year, with a slight boost in numbers from COVID-19 related trials.

Table 3. Top five diseases for trials completed in 2021, and comparison to prior three years

Disease	2021	2020	2019	2018
Novel coronavirus (2019-nCoV, COVID-19)	354 (1)	116 (9)	–	–
Non-small cell lung cancer	207 (2)	182 (1)	167 (4)	149 (4)
Respiratory infections	185 (3)	172 (2)	168 (3)	164 (3)
Breast cancer	164 (4)	165 (3)	174 (2)	179 (2)
Type 2 diabetes	155 (5)	161 (4)	222 (1)	211 (1)

Source: Trialtrove®, February 2022

Trial success rates

Completed trials are assigned an outcome evaluation (positive, negative, unknown, or indeterminate) when those studies report efficacy, or biomarker/surrogate efficacy outcomes, in the public domain. Success rates are calculated annually for diseases with the highest number of successful trials and ranked based on the percentage of their total completed trials (Table 4).

Table 4. Diseases with >25 completed trials attaining primary endpoint

Disease	I	I/II	II	II/III	III	III/IV	Total	% of all Trials	Rank#
Novel coronavirus (2019-nCoV, COVID-19)	36	12	39	15	18	0	120	33.9%	6
Non-small cell lung	24	11	30	1	21	0	87	42.0%	1
Breast	26	9	14	0	9	0	58	35.4%	5
Colorectal	22	8	15	0	4	0	49	37.1%	4
Non-Hodgkin's lymphoma*	11	6	19	0	4	0	40	28.8%	9
Respiratory infections	2	3	12	1	19	0	37	20.0%	14
Type 2 diabetes	14	1	5	0	17	0	37	23.9%	12
Prostate	9	4	13	0	7	0	33	32.0%	7
Esophageal*	8	2	13	0	8	0	31	41.9%	2
Ovarian*	12	6	9	0	3	0	30	30.3%	8
Gastric	10	3	11	0	5	0	29	38.7%	3
Head/Neck*	9	8	8	0	3	0	28	28.3%	10
Psoriasis	8	1	5	0	13	0	27	26.7%	11
Respiratory Vaccines	8	11	8	3	12	0	26	21.5%	13

**Rare disease*

Source: Trialtrove®, February 2022

 # Rank based on percentage of trials attaining primary outcome per disease.

Substantially fewer diseases achieved at least 25 successful trials in 2021 (14) compared with 2020 (21) and 2019 (17). COVID-19 dominated the field by this metric, with 120 trials reporting that primary endpoints were achieved. Respiratory vaccines made this list for the first time, based on 26 positive trials that included 22 for COVID-19 vaccines. Despite their relatively high trial counts, success ratings for these diseases are sixth and 13th, respectively, with Oncology indications taking the top five positions. The increasing trial activity in NSCLC, noted previously, has yielded 87 successful trials, and it both achieved the top ranking (42.0%) and outperformed success rates in both 2020 (39.6%) and 2019 (36.5%). Esophageal cancer is a very close second (41.9%) and reached essentially the same success rate as in 2020 (41.6%). Breast, colorectal, and gastric cancers completed 58, 49, and 29 positive trials, and ranked fifth (35.4%), fourth (37.1%), and third (38.7%), respectively. Other Oncology diseases occupy the 7–10 ranked positions, namely prostate, ovarian, head/neck cancer, and non-Hodgkin's lymphoma (NHL). Their trials returned success rates of 28.3–32.0%, which were lower than their 2020 rates. Three non-oncology diseases, psoriasis (26.7%), T2D (23.9%), and respiratory infections (20%), ranked at the positions of 11, 12, and 14. These diseases also ranked lowest in the 2020 analysis, but a further drop in their success rates was noted in 2021. The average success rate across all completed trials was 31.5%, compared with 33.0% in 2020. This year's average falls a bit higher than success rates over 2017–19 that ranged between 25.4% and 31.0%.

It is noteworthy that six diseases reported positive outcomes for at least 10 Phase III trials, which may support drug filings. The high activity diseases, COVID-19, NSCLC, T2D, and respiratory infections are among these, alongside the lower activity diseases of respiratory vaccines and psoriasis. In addition, trials for several rare diseases (esophageal, NHL, head/neck, and ovarian cancers) achieved primary endpoints in three or more Phase III trials, as well as even higher Phase II trial counts that also might support regulatory filings.

T2D, a disease within the Endo/Met TA, is notable for achieving double-digit successful Phase III trials for three consecutive years. In 2021, this included five registrational trials. Four global studies evaluated Eli Lilly's tirzepatide (the most advanced dual coagonist of gastric inhibitory polypeptide receptor and glucagon-like peptide-1 receptor in active development) and a pivotal trial conducted in South Korea for Daewoong Pharma's enavogliflozin, which is another sodium-glucose cotransporter-2 inhibitor. For the top TAs, Oncology, ID, and A/I, the successful pivotal trials will be explored in detail later in this analysis.

Leading Trial Sponsors

In previous years, we noted the relative contributions from top 20 pharma and a separate group comprising all other pharma (AOP), with these designations based on sales data in the annual In Vivo Outlook 2022 dataset.[4] In this year's analysis, a year-over-year shift was observed towards higher AOP contribution (and trial count): 65.2% (2,689) versus 62.9% (2,347) in 2020. Although the top 20 pharma set increased its overall completed trial counts (1,612 versus 1,575), the relative contribution to overall completed trials dropped from 41.6% to 39.6%. Please note that because trials can have multiple sponsors, these percentages do not necessarily sum to 100%. Within the individual clinical stages, the proportion of AOP sponsorship in Phase I was higher than observed in earlier analyses (data not shown). These shifts are mainly driven by the increased influx of Chinese Phase I trials, as noted previously, since these industry sponsors are all AOP companies.

Despite the shift towards smaller clinical trial sponsors, top 20 pharma continues to occupy the top five rankings for annual completed trial activity (Table 5). Bristol Myers Squibb (BMS) has moved steadily upwards since 2018 and is ranked at the top spot in 2021 with 177 completed trials. Compared with 2020, the rank order is nearly reversed, as Novartis has moved from first to fifth place and Pfizer has slipped from second to fourth place. AstraZeneca (AZ) has retained a top three ranking since 2018. Merck & Co. is the exception to this trend, rising from outside the top five in each of the last four years to achieve third position in 2021 for completed clinical trials. Several sponsors whose counts flattened in 2020 due to the pandemic have returned to growth trajectories evident between 2017 and 2019, including BMS, AZ, and Merck & Co. Conversely, Pfizer achieved its best performance in 2020 and has now returned to levels observed over 2017–19. Novartis has oscillated during the past five years, with 2021 marking a low point in its recent history.

Table 5. Top five sponsors* completing trials in 2017–21

Sponsor	2021 (rank)	2020 (rank)	2019 (rank)	2018 (rank)	2017 (rank)
Bristol Myers Squibb	177 (1)	139 (4)	141 (5)	78 (10)	–
AstraZeneca	175 (2)	142 (3)	179 (1)	156 (2)	138 (4)
Merck & Co.	140 (3)	127 (6)	125 (7)	114 (7)	110 (7)
Pfizer	134 (4)	152 (2)	137 (6)	131 (6)	135 (5)
Novartis	131 (5)	160 (1)	151 (3)	185 (1)	152 (3)

**Trial count includes co-sponsored trials.*

Source: Trialtrove®, February 2022

4. Informa Pharma Intelligence (2022) Pharma R&D Annual Review 2022. Available from: https://pages.pharmaintelligence.informa.com/rdreview [Accessed March 24, 2022].

Beyond the top five sponsors, 12 other sponsors completed 50 or more trials, comprising Eli Lilly (121), Roche (115), Johnson & Johnson (J&J; 110), Sanofi (82), GlaxoSmithKline (GSK; 80), AbbVie (76), Takeda (70), Boehringer Ingelheim (BI; 69), Jiangsu Hengrui Pharma (63), Otsuka (56), Bayer (53), and Amgen (52). Most of these sponsors met this criterion in 2020 but completed fewer trials in 2021. The most notable decrease was reported for Takeda (70 versus 101). J&J is the only sponsor to complete more trials in 2021 (110 versus 93). Two AOPs, Jiangsu Hengrui Pharma, and Otsuka, met the mark this year for the first time. Gilead completed only 33 trials in 2021, dropping well below the 59 trials it completed in each of the prior two years.

The performance of industry sponsors can also be evaluated by their overall counts of successful trials (Table 6) and by assessing success rates, calculated as the percentage of total completed trials that reported positive endpoints (Table 7). The number of sponsors reporting at least 25 positive trials decreased year-over-year from 11 to seven (Table 6). Most sponsors meeting this criterion were top 20 pharma, while the Chinese sponsor, Jiangsu Hengrui Pharma, is the exceptional AOP meeting this criterion. Eli Lilly returned to the list this year, while sponsors from last year that slipped below the threshold are Roche (24), Pfizer (21), Sanofi (19), AbbVie (19), Bayer (15), and Takeda (13). The spread between the highest and lowest positive trial counts (56 versus 27) is a bit narrower than that observed in 2020 (59 versus 25). The substantial drop in the number of sponsors attaining at least 25 positive trials drove a stark reduction in the positive trial count accounted for by this group, 266 versus 417, representing an annual -36.2% change.

Table 6. Companies attaining primary endpoints in >25 trials, by phase

Sponsor	I	I/II	II	II/III	III	III/IV	Total
AstraZeneca	12	5	21	1	17	0	56
Bristol Myers Squibb	7	7	22	1	8	0	45
Merck & Co.	5	5	12	1	15	0	38
Eli Lilly	9	2	6	1	18	0	36
Novartis	4	3	11	1	17	0	36
Johnson & Johnson	5	1	11	1	10	0	28
Jiangsu Hengrui Pharma	6	1	11	0	9	0	27

Source: Trialtrove®, February 2022

The number of sponsors (17) who completed at least 40 trials available to assess success rates remains unchanged over the past three years (Table 7). The highest success rate was achieved by Jiangsu Hengrui Pharma (42.9%), while the lowest rate was observed for Pfizer (15.7%). This year's top rate falls between the top rates achieved in 2020 and 2019 of 45.9% and 39.4%, respectively. Remarkably, Jiangsu Hengrui Pharma's success rate is nine percentage points above the nearest runner up, Otsuka (33.9%), while the increments between other sponsors'

success rates are much smaller. The average rate across these sponsors, 26.8%, represents a decrease compared with ~30% observed in the past two years. Nine of these sponsors performed above the average rate, while eight fell below it.

Most sponsors attained higher success rates in the later stages of drug development. This is likely an artefact of larger clinical trials being more likely to have their results reported in the public domain, and so are tagged as successful within Trialtrove.[5] Amgen is the only sponsor that showed a dip in its success rate from Phase II (37.5%) to Phase III (21.4%). The sponsors with high success rates in Phase III, and a substantial number of positive trials, are best positioned for potential filings, and include Jiangsu Hengrui Pharma, Otsuka, AZ, Eli Lilly, Novartis, Merck & Co., J&J, BMS, and BI. It is noteworthy that all of Jiangsu Hengrui Pharma's clinical trials were run in China, and only two of 27 successful trials also include any other countries. These other top sponsors mainly ran global trials.

Table 7. Percentage of 2021 trials* attaining primary endpoint, by phase, for companies completing >40 trials in 2021

Sponsor	I	I/II	II	II/III	III	III/IV	Total
Jiangsu Hengrui Pharma	17.6%	100.0%	68.8%		75.0%		42.9%
Otsuka	14.3%	50.0%	18.2%	100.0%	55.0%		33.9%
AstraZeneca	17.9%	31.3%	38.2%	50.0%	48.6%		32.0%
Eli Lilly	15.3%	28.6%	30.0%	100.0%	52.9%		29.8%
Amgen	15.8%	50.0%	37.5%	0.0%	21.4%		28.8%
Bayer	21.7%	0.0%	23.1%	0.0%	46.7%		28.3%
Novartis	19.0%	21.4%	18.6%	100.0%	47.2%		27.5%
GlaxoSmithKline	4.5%	28.6%	26.9%	100.0%	46.7%		27.5%
Merck & Co.	13.5%	25.0%	25.0%	50.0%	45.5%		27.1%
Johnson & Johnson	11.6%	14.3%	32.4%	100.0%	40.0%		25.5%
Bristol Myers Squibb	13.7%	28.0%	31.0%	20.0%	34.8%	0.0%	25.4%
AbbVie	20.0%	0.0%	11.8%	50.0%	39.4%		25.0%
Sanofi	10.0%	16.7%	20.0%	100.0%	32.4%	100.0%	23.2%
Boehringer Ingelheim	15.8%	0.0%	17.6%	0.0%	100.0%		23.2%
Roche	11.1%	7.7%	23.3%	100.0%	36.4%		20.9%
Takeda	9.1%	0.0%	25.0%	0.0%	30.0%	0.0%	18.6%
Pfizer	5.6%	10.0%	20.5%	0.0%	34.6%	0.0%	15.7%

**Trial count includes co-sponsored trials.*

Source: Trialtrove®, February 2022

5. New Clinical Development Success Rates 2011-2020 Report (2021) Available from: https://www.bio.org/clinical-development-success-rates-and-contributing-factors-2011-2020 [Accessed March 24, 2022].

Top Three Therapeutic Areas: Assessment by Top Sponsors, Diseases with Positive Pivotal Trials, and Pipeline Therapeutics

A deep dive in the most active TAs into successful sponsors, diseases, and drug programs elucidates trends at a more granular level. The top three TAs for completed trials in 2021 are Oncology, ID, and A/I. Historically, high trial activity in Oncology and A/I place these TAs in this group each year. However, the industry response to the COVID-19 pandemic drove ID trial activity to new heights, ensuring it reached top spot for the first time in 2021. Furthermore, across all of the TAs, the increased coverage universe and product enhancements within Trialtrove mean that a larger number of indications and patient segments can be tracked, particularly among new rare diseases.[6]

Oncology: Top sponsors, indications, and pipeline drugs in successful pivotal trials

The top 10 sponsors within Oncology are ranked by completed trial counts, assessed for success rates across all trial phases and their counts of positive pivotal trials (Table 8). This cast is dominated by top 20 pharma, including most of the same sponsors observed in prior years. However, in 2021, Bayer and Eli Lilly gave way to Amgen (rank nine) and Jiangsu Hengrui Pharma (rank eight). The number one sponsor again this year is BMS, with 118 trials, which exceeds its tallies from the past two years (97, 98). The second and third ranked sponsors also reported an increase; AZ completed 91 oncology studies in 2021 versus 83 in 2020, while Merck & Co. achieved 77 versus 64. Roche kept pace with its 2020 performance, with 67 completed trials, and retained fourth rank. Novartis dropped back to fifth rank, with a decrease from 78 to 61 trials. The relative rankings for Pfizer (6), J&J (7), and Takeda (10) are the same as in 2020, albeit with fewer trial completions.

Jiangsu Hengrui Pharma achieved the highest success rate, 45.7%, from 35 trials. This performance matches the top rate achieved in 2019 but is lower than the exceptional rate (64.0%) achieved by J&J in 2020. Only one sponsor matched its 2020 success rate, AstraZeneca (37.4% versus 36.1%). Most sponsors returned lower success rates, year-over-year, including BMS (32.2% versus 43.3%), Merck & Co. (32.5% versus 40.6%), Roche (19.4% versus 56.1%), Novartis (21.3% versus 29.5%), Pfizer (20.5% versus 26.5%), J&J (36.1% versus 64.0%), and Takeda (17.2% versus 27.8%). It is important to note that many sponsors have yet to fully report results (Outcomes indeterminant or Unknown). When fuller details are disclosed, these trials can be assigned either a positive or negative outcome, which will change this picture. The sum of top sponsors' trial counts (588) exceeds the 2020 count (552), but the average success rate (30.2%) has continued to decline since 2019 (2020, 36.4%; 2019, 39.6%).

6. Oncology - penile, vaginal, vulvar, fallopian tube, anal, primary peritoneal, bile duct (cholangiocarcinoma), and gallbladder cancers; A/I - dermatomyositis/polymyositis, hidradenitis suppurativa, immune thrombocytopenia (ITP); Met/Endo - metachromatic leukodystrophy (MLD), polycystic kidney disease (PKD), Alport syndrome, IgA nephropathy, Pompe disease, Alagille syndrome; CV - neurogenic orthostatic hypotension (nOH); Vaccines: shigella, tuberculosis; CNS - neuromyelitis optica spectrum disorder (NMOSD); Ophthalmology - choroideremia

An important milestone in clinical development programs is pivotal trials that meet primary endpoints, which may support new regulatory filings. BMS achieved success in six pivotal trials, making it the top performer by this measure again this year. AZ (5) and Merck & Co. (4) have notable counts of these, as well. Five sponsors reported success in two pivotal studies, and Pfizer reported success in a single pivotal trial. Only Amgen reported no positive results for pivotal trials during this period.

Table 8. Top 10 sponsors with completed oncology trials, by success rates and positive pivotal trial counts

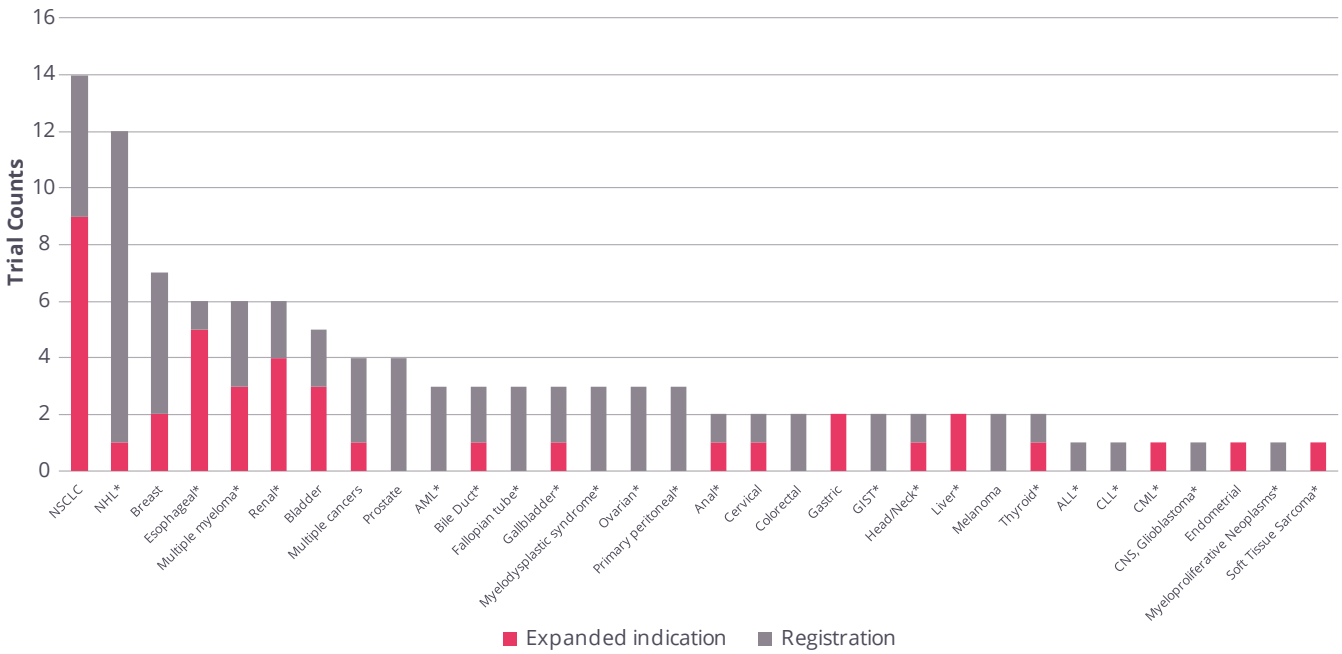
Sponsor	Negative outcome/ primary endpoints not met	Outcome indeter-minate	Outcome unknown	Early positive outcome	Positive outcome/ primary endpoints met	NA	Total Trials (rank)	Success Rate	Positive Pivotal Trials (count)
Bristol Myers Squibb	13	27	40	1	37	0	118 (1)	32.2%	6
AstraZeneca	6	17	30	4	30	4	91 (2)	37.4%	5
Merck & Co.	3	21	25	3	22	2	77 (3)	32.5%	4
Roche	4	14	32	1	12	4	67 (4)	19.4%	2
Novartis	4	21	23	0	13	0	61 (5)	21.3%	2
Pfizer	2	20	11	0	9	2	44 (6)	20.5%	1
Johnson & Johnson	1	5	14	0	13	3	36 (7)	36.1%	2
Jiangsu Hengrui Pharma	0	0	12	1	21	1	35 (8)	45.7%	2
Amgen	1	4	10	1	11	3	30 (9)	40.0%	0
Takeda	3	12	7	1	4	1	29 (10)	17.2%	2

Source: Trialtrove®, February 2022

Note: Indeterminate designation is assigned to trials when the outcome is neither clearly positive nor negative. Unknown is assigned to trials that have yet to report full results for their primary endpoints. NA indicates trials with no efficacy/safety outcomes to evaluate.

The focus now shifts to the disease level, where successful pivotal studies spanned 32 diseases from a total of 51 in Oncology, including 21 rare diseases. Note that trials enrolling more than one disease are counted for each individual disease on the graph (Figure 4). These were split between 51 registration (first approval) and 33 expanded indication trials. This tally of successful pivotal trials (84) exceeds the number in 2020 (71) and was augmented by trials in rare cancer indications such as bile duct, gallbladder, fallopian tube, primary peritoneal, and anal cancers. The highest activity indications, NSCLC, NHL, breast cancer, and multiple myeloma, retain the top spots again this year, with both registration and label expansion strategies being pursued. Top 20 pharma sponsored 32 of these trials (38.1%) and AOP sponsored 52 studies (61.9%). The top 20 pharma's trials were conducted globally, with one exception: a single-country Japanese Roche/Chugai study. By contrast, the AOP-sponsored trials are a blend of single-country trials in China (23), Japan (four), and the US (one), as well as global, or multinational, trials (24) (data not shown).

Figure 4. Pivotal oncology trials achieving primary endpoints, by disease and filing type



Source: Trialtrove®, February 2022

**Rare disease*

ALL = acute lymphoblastic leukemia; AML = acute myelogenous leukemia; CLL = chronic lymphocytic leukemia; CML = chronic myelogenous leukemia; NHL = non-Hodgkin's lymphoma; NSCLC = non-small cell lung cancer

Within the segment of successful pivotal oncology trials in 2021, there are 26 different pipeline candidates that have yet to launch in any market. These investigational drugs and their mechanisms of action (MOAs) are identified in Table 9. There were nine drugs with a novel MOA, as determined from their Pharmaprojects profiles. Most of these candidates (six) were successful in rare cancers, while 177Lu-PSMA-617, plinabulin, and relatlimab + nivolumab were evaluated in more prevalent cancers (prostate, breast, NSCLC, and melanoma). The other 17 drugs employ a variety of proven MOAs, including familiar targets for breast, prostate, colorectal, and NSCLC. The most common MOA among this set is PD-1 antagonism. These drugs are considered "me-too" candidates, as they have a proven MOA and are in development for the same indications already approved for the first-in-class versions.

Table 9 also highlights the drugs that have been evaluated in single-country trials, revealing that eight trials ran in China (pink fill) and three trials were conducted solely in Japan (gray fill). Most of the other candidates (13) reported success in multinational trials that could support broad regulatory filings. Trials for two novel candidates, Incyte's therapeutic cancer vaccine maveropepimut-S and Chimerix's ONC-201, were conducted only in Canada/US and the US, respectively.

Table 9. Pipeline status drugs in successful pivotal oncology trials, by sponsor, disease, MOA, and MOA novelty

Drug name	Sponsor	Disease	Mechanism of Action	Novel
177Lu-PSMA-617	Novartis	Prostate	PSMA targeted radioligand therapy	Yes
mirvetuximab soravtansine	ImmunoGen	Fallopian Tube*/ Ovarian*/Peritoneal*	Folate receptor alpha	Yes
momelotinib	Sierra Oncology	Myeloproliferative Neoplasms*	Activin R-like kinase 2/ JAK1/2 inhibitor	Yes
maveropepimut-S	Incyte/IMV Inc.	Fallopian Tube*/ Ovarian*/Peritoneal*	Survivin-based antigens (vaccine)	Yes
ONC-201, Chimerix	Chimerix/Oncoceutics	Glioblastoma*	Dopamine D2 R antagonist/ClpP agonist	Yes
plinabulin	BeyondSpring/Dalian Wanchunbulin/ Pharmaceutics International	Breast/ NSCLC/Prostate	Rho/Rac GNEF2 stimulant; Tubulin inhibitor	Yes
relatlimab + nivolumab	Bristol Myers Squibb	Melanoma	LAG-3 antagonist/PD-1 antagonist	Yes
tazemetostat	Eisai	NHL*	Enhancer of zeste homolog 2 inhibitor	Yes
valemetostat	Daiichi Sankyo	ALL*/CLL*/NHL*	Enhancer of zeste homologs 1/2 inhibitor	Yes

elacestrant	Menarini Group	Breast	Estrogen receptor downregulator	No
felzartamab	Thermo Fisher/I-Mab Biopharma	Multiple Myeloma*	CD38 antagonist	No
futibatinib	Otsuka	Multiple solid tumors	FGF receptor PKI	No
genolimzumab	Genor	NHL*	PD-1 antagonist	No
linperlisib	Shanghai Yingli Pharma	NHL*	PI3 kinase delta inhibitor	No
margetuximab	Baxter/MacroGenics/ Zai Lab	Breast	ErbB2 antagonist (biobetter)	No
parsaclisib	Incyte	NHL*	PI3 kinase delta inhibitor	No
pimitespib	Otsuka	GIST*	HSP90 antagonist	No
poziotinib	Spectrum Pharma	NSCLC	ErbB 2/3/4 inhibitor	No
pucotenlimab	Akeso Biopharma	Melanoma/Multiple solid tumors	PD-1 antagonist	No
retifanlimab	Incyte	Anal*	PD-1 antagonist	No
savolitinib	Hutchmed	NSCLC	cMet PKI	No
serplulimab	Shanghai Henlius Biotech	Multiple solid tumors	PD-1 antagonist	No
SHR-3680	Jiangsu Hengrui Pharma	Prostate	Androgen receptor antagonist	No
Therasphere	Boston Scientific	Colorectal	DNA inhibitor (radiopharmaceutical)	No
tipifarnib	Kura Oncology	Multiple solid tumors	Farnesyltransferase inhibitor	No
trastuzumab duocarmazine	Byondis	Breast	Anti-HER2 mAb-drug conjugate	No

Source: Trialtrove® and Pharmaprojects®, February 2022

**Rare disease*

Gray fill: Japan only trial; Pink fill: China only trial

Activin R = activin receptor; ALL = acute lymphoblastic leukemia; CLL = chronic lymphocytic leukemia; ClpP = mitochondrial protease ClpP; FGF = fibroblast growth factor; GNEF2 = guanine nucleotide exchange factor 2; HSP90 = heat shock protein 90; JAK1/2 = Janus kinases 1 and 2; LAG-3 = lymphocyte-activation gene 3 antagonist; mAb = monoclonal antibody; NHL = non-Hodgkin's lymphoma; NSCLC = non-small cell lung cancer; PD-1 = programmed death-1; Peritoneal = primary peritoneal; PI3 = phosphoinositide 3; PKI = protein kinase inhibitor; PSMA = prostate-specific membrane antigen

Infectious diseases: Top sponsors, indications, and pipeline drugs in successful pivotal trials

Infectious diseases joined the top three TAs, as COVID-19 related trial activity generated a high number of completed trials in the second year of the pandemic. The top ID sponsors include 10 top 20 pharma and two AOPs (ViiV Healthcare, China National Pharma). The spread between the sponsors by trial completions, success rates, and pivotal trial reporting success is broad. At the top ranking, Merck & Co., Pfizer, and GSK completed similar numbers of trials – 48, 47, and 45, respectively. These sponsors attained success rates below 23%, but all have reported success in at least two pivotal trials. At the lowest rank, Eli Lilly returned a 33.3% success rate from nine completed trials and reported one successful pivotal trial. Among the mid-ranked sponsors, AZ had the highest success rating (40.0%) from 15 completed trials, including two successful pivotal studies. Roche achieved a lower success rate (6.7%) from its 15 completed trials, while also reporting success in one pivotal trial. The remaining top sponsors of ID trials – J&J, Sanofi, ViiV Healthcare, Gilead, Novartis, and China National Pharma – achieved success rates of 5.3–30.8% but reported no positive pivotal trials during 2021. The average success rate across all of the top sponsors was 19.5%, and five of 12 sponsors exceeded this rate. Considering the substantial number of trials with indeterminant or unknown outcomes, the performance profiles are likely to change once full results are disclosed.

Table 10. Top sponsors with completed infectious disease trials, by success rates and positive pivotal trial counts

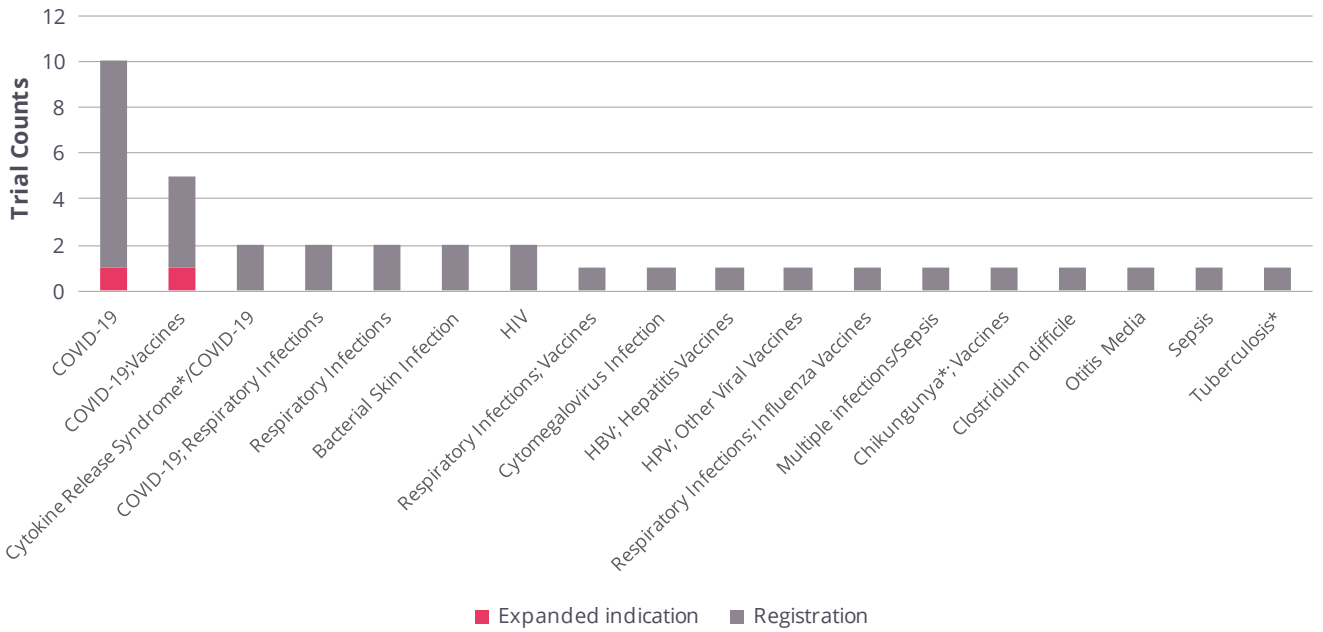
Sponsor	Negative outcome/ primary endpoints not met	Outcome indeter-minate	Outcome unknown	Early positive outcome	Positive outcome/ primary endpoints met	NA	Total Trials (rank)	Success Rate	Positive Pivotal Trials (count)
Merck & Co.	0	16	13	1	9	9	48 (1)	20.8%	4
Pfizer	4	5	14	1	6	17	47 (2)	14.9%	2
GlaxoSmith-Kline	2	7	17	1	9	9	45 (3)	22.2%	2
Johnson & Johnson	0	5	14	0	5	4	28 (4)	17.9%	0
Sanofi	2	4	11	0	1	1	19 (5)	5.3%	0
ViiV Healthcare	2	1	2	0	3	8	16 (6)	18.8%	0
Roche	2	4	2	0	1	6	15 (7)	6.7%	1
AstraZeneca	4	0	4	1	5	1	15 (7)	40.0%	2
Gilead	1	3	7	0	1	3	15 (7)	6.7%	0
Novartis	2	3	3	0	4	1	13 (8)	30.8%	0
China National Pharma	0	0	9	0	2	1	12 (9)	16.7%	0
Eli Lilly	1	2	2	0	3	1	9 (10)	33.3%	1

Source: Trialtrove®, February 2022

Note: Indeterminate designation is assigned to trials when the outcome is neither clearly positive nor negative. Unknown is assigned to trials that have yet to report full results for their primary endpoints. NA indicates trials with no efficacy/safety outcomes to evaluate.

At the disease level, successful pivotal trials were reported for 15 of 34 ID diseases. From 36 pivotal ID studies, 19 evaluated COVID-19 treatment, complications, prevention, or vaccines (Figure 5). Two trials are considered expanded indication studies, one for Moderna's COVID-19 vaccine in adolescents and another for Kineret in COVID-19 treatment. The other pivotal trials are for first filings, as is typical for targeted vaccines, new antiviral medications, and antibiotics. Among the successful registration trials, two were studies for cytokine release syndrome, which is a rare A/I disease and a complication of COVID-19 infection. Top 20 pharma sponsored 13 of these successful pivotal trials (36.1%), and AOP sponsored 23 studies (63.9%) (data not shown).

Figure 5. Pivotal infectious disease trials achieving primary endpoints, by disease and filing type



**Rare disease*

Source: Trialtrove®, February 2022

The ID drug analysis is focused on the unapproved candidates that achieved primary endpoints in registration trials and identifies those with novel and me-too MOAs. Considering the dominance of COVID-19 therapeutics this year, it is not surprising that 16 of 29 pipeline drugs were successful in this indication. COVID-19 vaccines, COVID-19 anti-surface GP antibodies, and SARS 3 cysteine-like protease inhibitors are considered novel as they were developed specifically for these new viral targets. The 13 highlighted drugs are those evaluated in single-country trials, including in Brazil, India, Japan, Russia, South Korea, Turkey, and the US (chikungunya vaccine). These are exclusively AOP-sponsored candidates, while the remainder were tested in trials conducted globally and were sponsored by both top 20 pharma (10) and AOP (six) companies.

Table 11. Pipeline status drugs in successful pivotal infectious disease trials, by sponsor, disease, MOA, and MOA novelty

Drug name	Sponsor	Disease	Mechanism of Action	Novel
COVID-19 vaccine	Sinovac Biotech	COVID-19 (vaccine)	Immunostimulant	Yes
COVID-19 vaccine	Noravax	COVID-19 (vaccine)	Immunostimulant	Yes
COVID-19 vaccine/ adjuvant	Medicago	COVID-19 (vaccine)	Immunostimulant	Yes
ritonavir/ nirmatrelvir	Pfizer	COVID-19 (treatment)	P450 inhibitor/SARS 3 CLPI	Yes
lenzilumab	Humanigen	COVID-19 (critical/ complications)*	GMCSF antagonist	Yes
VIR-7831	GSK/Vir Biotech	COVID-19 (treatment)	Surface GP (SARS-CoV-2) antagonist	Yes
bamlanivimab/ etesevimab	Eli Lilly	COVID-19 (treatment)	Surface GP (SARS-CoV-2) antagonist	Yes
cilgavimab/ tixagevimab	AstraZeneca	COVID-19 (treatment)	Surface GP (SARS-CoV-2) antagonist	Yes
regdanvimab	Celltrion	COVID-19 (treatment)	Surface GP (SARS-CoV-2) antagonist	Yes
casirivimab/ imdevimab	Regeneron/Roche	COVID-19 (treatment)	Surface GP (SARS-CoV-2) antagonist	Yes
aviptadil	NRx Pharmaceuticals	COVID-19 (critical/ complications)*	VIP agonist	No
chikungunya vaccine	Valneva	Chikungunya*	Immunostimulant	No
doravirine/ islatravir	Merck & Co.	HIV	Non-nucleoside RTI/ Nucleoside RTI	No
HPV vaccine	Inovio Pharma	HPV	Immunostimulant	No
levilimab	Biocad Biotech	COVID-19 (severe)	IL-6R antagonist	No
maribavir	Takeda	Cytomegalovirus Infection	CMV UL97 PKI	No

MEDI-8897	AstraZeneca	Respiratory Infections (RSV)	Immunostimulant	No
molnupiravir	Merck & Co.	COVID-19 (treatment)	Viral replication inhibitor	No
nafamostat mesilate	Chong Kun Dang Pharma	COVID-19 (pneumonia)	Kallikrein inhibitor	No
pneumococcal vaccine, 15-valent	Merck & Co.	Respiratory Infections	Immunostimulant	No
proxalutamide	Applied Biology/ Kintor Pharma	COVID-19 (treatment)	Androgen receptor antagonist	No
rezafungin acetate	Cidara Thera	Sepsis	1,3-Beta-glucan synthase inhibitor	No
seasonal influenza vaccine	Medicago	Respiratory Infections	Immunostimulant	No
SER-109	Seres Thera	Clostridium difficile	Microbiome modulator	No
SQ-109	Infectex	Tuberculosis*	MmpL3 inhibitor	No
sulbactam-durlobactam	Zai Lab/Entasis Thera	Multiple bacterial infections	Lactamase-A/C inhibitor	No
ENT-103	Ceolia Pharma	Otitis media	Unidentified	N/A
pHOXWELL	Raphael Labs/ pHOXBIO	COVID-19 (Exposure prophylaxis)	Unidentified	N/A
ZuraPrep	Zurex	Bacterial skin infection	Unidentified	N/A

Source: Trialtrove® and Pharmaprojects®, February 2022

**Rare disease*

Gray fill: single-country studies sponsored by AOP

CLPI = cysteine-like protease inhibitor; GP = glycoprotein; IL-6R = IL-6 receptor; P450 = cytochrome P450; PKI = protein kinase inhibitor

Autoimmune/Inflammation: Top sponsors, indications, and pipeline drugs in successful pivotal trials

In the A/I space, there is a high degree of consistency among leading sponsors of completed clinical trials (Table 10). The same companies continue to claim the top 10 positions over the past three years, with only one new sponsor in 2021, Galapagos. Two former top A/I sponsors are no longer on this list as their development programs are largely completed; Chiesi developed inhaled drugs for asthma and chronic obstructive pulmonary disease, while Gilead has ceased its partnership with Galapagos for the investigation of filgotinib in inflammatory diseases.

The relative placement for most sponsors has shifted, except for Pfizer, who retained its third ranking. BMS achieved first rank in A/I for the first time, with 33 trials, which is lower than the highest counts recorded in 2020 (35) and 2019 (48). Last year's top sponsor, Novartis, moved to

second rank (30) as it continues a decline in A/I completions observed since 2019. Downward trends also were observed for Pfizer, AbbVie, AZ, Roche, and GSK. Only BMS, BI, Eli Lilly, and Sanofi completed more trials than in 2020. Across A/I's top sponsors the total number of completions dropped to 249, from 262 (2020) and 327 (2019).

AbbVie retains its position as A/I's top sponsor by success rate, albeit with a lower score than in the past year (50.0% versus 77.8%). Other sponsors that slipped in their annual rates include BMS (15.2% versus 55.0%), Novartis (23.3% versus 31.4%), Pfizer (14.8% versus 18.8%), BI (12.5% versus 20.0%), and Eli Lilly (34.8% versus 35.7%). Several sponsors improved their rates this year: AZ (31.8% versus 24.0%), Sanofi (25.0% versus 20.0%), and GSK (28.6% versus 16.0%). The average success rate for top A/I companies (25.7%) falls between the averages reported in the previous two years, 28.2% and 22.0%.

Eight of 11 sponsors completed at least one positive pivotal trial, while AZ, Galapagos, and GSK reported no positive pivotal trials in 2021. Eli Lilly, AbbVie, Novartis, BI, and Pfizer each achieved primary endpoints in at least two pivotal trials.

Table 12. Top 10 sponsors with completed autoimmune/inflammation trials, by success rates and positive pivotal trial counts

Sponsor	Negative outcome/ primary endpoints not met	Outcome indeter-minate	Outcome unknown	Early positive outcome	Positive outcome/ primary endpoints met	NA	Total Trials (rank)	Success Rate	Positive Pivotal Trials (count)
Bristol Myers Squibb	1	6	9	0	5	12	33 (1)	15.2%	1
Novartis	3	8	7	0	7	5	30 (2)	23.3%	4
Pfizer	1	4	11	0	4	7	27 (3)	14.8%	2
AbbVie	3	5	5	0	13	0	26 (4)	50.0%	6
Boehringer Ingelheim	1	2	10	0	3	8	24 (5)	12.5%	3
Eli Lilly	1	1	7	0	8	6	23 (6)	34.8%	7
AstraZeneca	2	3	6	0	7	4	22 (7)	31.8%	0
Roche	4	2	5	0	4	3	18 (8)	22.2%	1
Sanofi	1	6	3	0	4	2	16 (9)	25.0%	1
Galapagos*	1	1	4	0	4	6	16 (9)	25.0%	0
GlaxoSmith-Kline	0	4	5	0	4	1	14 (10)	28.6%	0

Source: Trialtrove®, February 2022

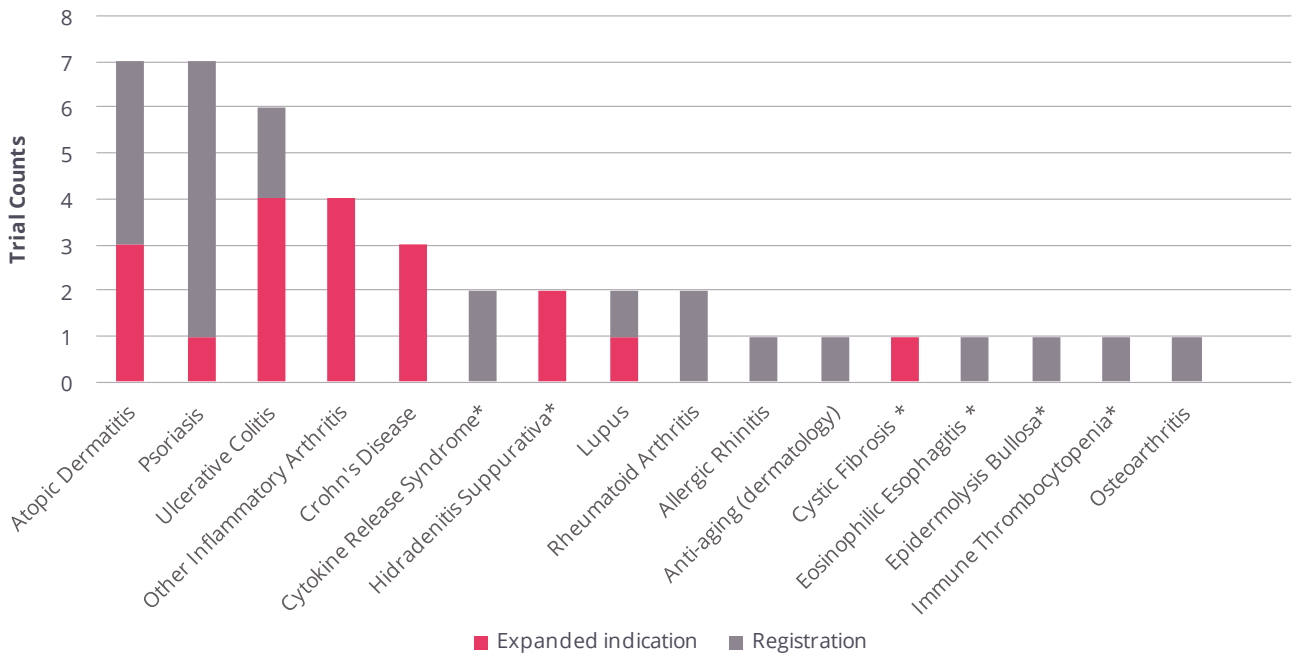
Note: Indeterminate designation is assigned to trials when the outcome is neither clearly positive nor negative. Unknown is assigned to trials that have yet to report full results for their primary endpoints. NA indicates trials with no efficacy/safety outcomes to evaluate.

**Includes four co-sponsored trials with Gilead.*

Successful pivotal studies were reported in 16 of 32 diseases in the A/I portfolio (Figure 6). Psoriasis and atopic dermatitis retained the top spots for the most completed trials. The trial completions in ulcerative colitis (UC) surpassed those for rheumatology indications this year for the first time. This UC research included successful label expansions trials for mirikizumab, tofacitinib, and upadacitinib. Two successful secukinumab trials for the rare disease of hidradenitis suppurativa are also expanded indications studies. Cytokine release syndrome (CRS) is a complication sometimes caused by COVID-19; therefore, the successful trials reported are related to pandemic trial activity.

The pivotal trials tally (42), including 23 registration and 19 expanded indication trials, was lower than that of 2020 (53). Top 20 pharma sponsored 23 positive pivotal trials (54.8%), and 19 were sponsored solely by AOP sponsors (45.2%) (data not shown). All top 20 sponsored trials were global or multinational. For AOP-sponsored studies, eight studies were run in Japan and China, while 11 trials were global or multinational.

Figure 6. Pivotal autoimmune/inflammation trials achieving primary endpoints, by disease and filing type



**Rare disease*

Source: Trialtrove®, February 2022

Within the A/I pipeline, there are 14 drugs that successfully completed registration trials during 2021. Half of these successful candidates have novel MOAs, while the other half are "me-too" therapies with proven MOAs. Dermatology indications including psoriasis, atopic dermatitis, anti-aging, and epidermolysis bullosa (EB) are the focus of 43.8% (six) of these pivotal studies.

Several novel cytokine pathway antagonists include BI's IL-36 receptor antagonist BI655130 and BMS's tyk2 inhibitor deucravacitinib, which blocks both IL-12/IL-23 and type I interferon signaling. Both drugs are being evaluated in multiple indications beyond psoriasis, including UC, Crohn's disease, lupus, atopic dermatitis, hidradenitis suppurativa, and psoriatic arthritis. These studies have yet to report positive results beyond a single positive Phase II study for deucravacitinib in psoriatic arthritis.

Novel candidates also were positive for three rare diseases: CRS, EB, and eosinophilic esophagitis. The "cytokine storm" caused by COVID-19 infection also occurs in response to some oncology therapies; therefore, Humanigen's GMCSF antagonist lenzilumab might have broader therapeutic utility. EB is a group of rare diseases caused by autosomal mutations, thus bercolagene telserpavec is a very targeted therapy for this condition alone. The SIGLEC inhibitors, including Allakos's lirentelimab, may become a treatment for a variety of dermatological and eosinophilic diseases which are now under clinical investigation.

Among the drugs that are not first-in-class, and are focused on dermatology indications, candidates include an anti-IL-13, lebrikizumab, and another IL-17 pathway antagonist, UCB's UCB4940. Single-country studies comprised Eisai's Japanese carotegrast methyl study, as well as China-only trials for Genor's infliximab biosimilar and Daewoong Pharma's botulinum toxin biosimilar.

Table 13. Pipeline status drugs in successful pivotal autoimmune/inflammation trials, by sponsor, disease, MOA, and MOA novelty

Drug name	Sponsor	Disease	Mechanism of Action	Novel
bercolagene telserpavec	Krystal Biotech	Epidermolysis Bullosa*	Collagen stimulant	Yes
BI655130	Boehringer Ingelheim	Psoriasis	IL-36 receptor antagonist	Yes
carotegrast methyl	Kissei Pharma/Eisai	Ulcerative colitis	Alpha4 integrin antagonist	Yes
deucravacitinib	Bristol Myers Squibb	Psoriasis	Tyk2 inhibitor	Yes
diketopiperazines	Ampio	Osteoarthritis/Pain	Unknown	Yes
lenzilumab	Humanigen	Cytokine release syndrome*	GMCSF antagonist	Yes
lirentelimab	Allakos	Eosinophilic Esophagitis*	Siglecs inhibitor	Yes
AM-301	Altamira Thera	Allergic Rhinitis	Specific immunotherapy	No

aviptadil	NRx Pharmaceuticals	Cytokine release syndrome*	VIP agonist	No
infliximab (biosimilar)	Genor	Rheumatoid Arthritis	TNFalpha antagonist	No
lebrikizumab	Eli Lilly/Dermira/ Almirall	Atopic dermatitis	IL-13 antagonist	No
prabotulinum toxin A	Daewoong Pharma	Anti-aging (dermatology)	Acetylcholine release inhibitor	No
UCB4940	UCB	Psoriasis	IL-17A antagonist	No
voclosporin	Aurinia Pharma/ Otsuka	Lupus (nephritis)	Calcineurin inhibitor	No

Source: Trialtrove® and Pharmaprojects®, February 2022

**Rare disease*

Gray fill: Japan only trial; Pink fill: China only trial

GMCSF = granulocyte-macrophage colony-stimulating factor; IL-13 = interleukin 13; IL-17A = interleukin 17A; IL-36 = interleukin 36; SIGLEC = Sialic acid binding lg-like lectin; Tyk2 = tyrosine kinase 2; VIP agonist = vasoactive intestinal polypeptide agonist

Key Takeaways

Our annual completed trials analyses reported continuous growth until 2020, when the COVID-19 pandemic caused high numbers of trial terminations and delayed ongoing trials, effectively driving trial completions to lower levels. During this second pandemic year, overall trial completions returned to growth with an 8.8% increase. The high volume of COVID-19 trials within the ID and Vaccines TAs is responsible for most of this improvement, while Oncology's 8.3% growth rate was another contributor to this increase. Conversely, several TAs including A/I, CNS, Met/Endo, CV, and Ophthalmology reached inflexion points in 2020 as pandemic-related impacts drove declining trial completions. Only A/I and Ophthalmology returned to growth in 2021, suggesting continued challenges in the lagging TAs. Pandemic-related impacts for delayed ongoing trials increased in the past year, most notably in Oncology, which runs longer trials, thus its delays became more evident in the second pandemic year. The TAs with the highest percentage of rare disease trials experienced delays that mainly were due to slow recruitment and trial suspensions, as might be expected for studies in these small and vulnerable populations. Terminations increased only in ID and Vaccines, where the main reasons reported in COVID-19 trials were poor enrollment and logistical challenges. Clearly, the pandemic impacts continued to be felt throughout the past year and reshaped the completed trials trends.

Aside from the large number of ID trial completions, growth also was traced to a marked increase in Chinese clinical trials, reaching a

tally of 599 completed trials. These trials were sponsored by local sponsors and conducted exclusively in China. While 68.1% of these were relatively short Phase I trials, this trend also points to how COVID-19 impacted China much earlier than in the West and reflects how quickly normal clinical operations were able to recover.

Despite the overall increase in completed trial counts, fewer diseases reported high numbers of successful trials, and average success rates were lower than in the past year. The prevalent diseases of NSCLC, breast cancer, T2D, and respiratory infections still met the cut off of at least 25 positive trials reported, but completed fewer positive trials. In 2020, new non-Oncology diseases met this criterion, including dyslipidemia, atopic dermatitis, and non-alcoholic fatty liver disease (NAFLD), but did not have sufficient successful trials to hold their place in 2021. Nevertheless, the overall success rate across TAs of 31.5% was nearly the same as that attained in 2019. Trialtrove's new rare disease product enhancement was used to reveal the magnitude of research in the less prevalent diseases. Most notably, in Oncology, successful pivotal trials were reported for 21 rare diseases, and, in A/I, these were reported for five rare diseases. For COVID-19 trials, the average success rate was lower than last year, 33.9% versus 35.2%. However, clinical activity was fruitful and additional antiviral therapies, beyond the familiar vaccines, were successful. Several COVID-19 treatment drugs were developed in record time, including AZ's cilgavimab/tixagevimab, Celltrion's regdanvimab, Roche's casirivimab/imdevimab, and Eli Lilly's bamlanivimab and etesevimab, which also were successful as a combination therapy. It will be interesting to follow ID in the coming years as the pandemic wave attenuates and more COVID-19 trials report their outcomes.

The granular analyses for the top three TAs highlighted the geographic scope of successful pivotal trials. Many AOPs were successful with single-country domestic trials, indicating that approval applications will be filed locally. In Oncology and A/I, novel candidates were evaluated in Japan, including Daiichi Sankyo's valemetostat and two by Eisai (tazemetostat and carotegrast methyl). Beyond those drugs, the single-country studies in Oncology and A/I were conducted in China and evaluated "me-too" candidates that might serve the local market. For example, the Chinese AOP Jiangsu Hengrui Pharma reported the highest success rate (42.9%) from 63 completed trials. The company's geographic focus was exclusively in China, and its successful trials evaluated a trastuzumab biosimilar, a PD-1 antagonist (camrelizumab), an androgen receptor antagonist, and several PKIs. For ID, single-country trials ran in a broader range of countries and were successful both in COVID-19 and other infectious diseases.

Across all TAs, studies sponsored by top 20 pharma were conducted globally, thus could have the broadest impacts. No sponsor succeeded in registration trials for pipeline drugs in all three leading TAs, as Novartis did in 2020. However, BMS is the top sponsor overall with 177 completed trials and an approximate one-in-four success rate. In Oncology and A/I, BMS's pivotal trials achieved primary endpoints for novel therapeutics in melanoma (relatlimab + nivolumab) and psoriasis (deucravacitinib). AstraZeneca's consistently high performance placed it again among the top five sponsors,

while Merck & Co. joined this list for the first time in our analyses. Both AZ and Merck & Co. completed successful pivotal trials in ID and Oncology. AZ's COVID-19 treatment was a novel therapy, while its Oncology research included four expanded indication studies. Merck & Co. also contributed new candidates to ID, including an influenza vaccine and viral inhibitors of HIV and COVID-19, and its Oncology research was likewise focused on label expansions. Eli Lilly, though not among the top five sponsors, was an important contributor in ID and A/I. The company's novel COVID-19 treatment mAbs have already reached the market, and lebrikizumab, an IL-13 antagonist, was successful in global atopic dermatitis trials. Novartis, Roche, and Pfizer are highly active in the top three TAs but completed pivotal trials for new candidates in only one TA. Novartis's successful pivotal trial was for a novel radiolabeled anti-PSMA drug for prostate cancer, while Roche and Pfizer made contributions with their novel COVID-19 therapies.

Balancing the relative contributions of the top 20 pharma, it can be concluded that these sponsors remain essential for the development of novel medicines at the global level. Nevertheless, the remaining smaller pharma companies possess an increasing share of clinical activity and are important for domestic approvals. In recent years, there is a growing list of larger US- and EU-headquartered organizations that are completing fewer studies, only to be replaced by emerging companies in China and Japan with narrower therapeutic and geographic focuses.

About The Author

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Laura has over 30 years of experience within the pharma industry and academia, and currently supports clinical trial intelligence for the autoimmune/inflammation, CNS, and ophthalmology therapeutic areas at Citeline. She has contributed to many Citeline thought leadership pieces, including the annual completed trials analysis since 2017. Prior to joining Citeline in 2006, Laura performed research focused on immunology, HBV, and gene regulation.

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