

2017 Clinical Trials Roundup: The Evolution Continues



Introduction

The landscape of clinical trials continues to evolve over time as scientific breakthroughs and technological innovations emerge, which continue to be tracked by assessing recently initiated trials through Trialtrove's annual Clinical Trials Roundup. Assessing the landscape of Phase I–III clinical trials that initiated in the previous year provides insights into competitive trial landscape, revealing priorities and strategies of the industry at large, as well as individual companies. Just as industry trends shift, the roundup has also changed over time, including last year's expansion to include all drugs in active

development across all therapeutic areas (TAs) covered by Trialtrove.

In this year's analysis, we'll continue to evaluate a more comprehensive landscape, dissecting the data of all Phase I–III clinical trials that started within 2017, regardless of the primary drug status. As usual, we'll begin with metrics by TA, trial phase, and disease, then zoom in on the most active industry sponsors, before wrapping up the roundup with a geographical survey of trial activity.

The Progeny of 2017 Trial Activity

As of June 6, 2018, Trialtrove captured 6,794 Phase I to III clinical trials investigating at least one drug initiated within 2017. Despite an earlier snapshot date, this figure slightly exceeds the number of 2016 trial starts, which stood at 6,067 as of July 6, 2017.¹

Many of the trends remain in line with last year's analysis. The majority of trials starting in 2017 continue to include at least one unapproved² primary drug, and at the same proportion observed for the 2016 trial starts (57%) (see Figure 1: Drug approval status). Oncology remains the most active TA³, and is still outpacing the runner-up, CNS, with nearly three times more activity (2,868 for oncology versus 1,003 for CNS). Autoimmune/Inflammation (A/I) also retains its ranking as the third most active TA. In fact, the rankings for all TAs remain the same, except for two – metabolic/endocrinology (metabolic) and infectious disease (ID)⁴ (see Figure 1: Therapeutic areas by rank order).

While trial activity increased overall, and in nearly all TAs, a marked decrease is observed for ID, resulting in the ranking switch with metabolic (Figure 1: Therapeutic areas by rank order). This shrinkage is a parallel to the observed decline in the number of anti-infective drugs in active development; according to the 2018 Pharma R&D Review, a 9.3% decrease was observed between 2017 and 2018.⁵ Although HCV stole the show in recent years with significant advances in treatments effectively curing patients, the area has retracted due to falling patient numbers, and falling prices due to a competitive market. With the declining market, pipeline interest has also declined, along with reduced new trial activity. HIV is another area with declining new activity, likely due to the saturation of single-tablet regimens (STRs) launched by Gilead, as well as expected readouts of pivotal STR trials for ViiV Healthcare, both of which are expected to enter the market in the near future, offsetting the imminent need for new clinical research.⁶

1. At the time of writing, the number of trial starts for 2016 has increased to 7,129 as a result of sponsor delays in reporting. For more detail regarding delayed reporting of clinical trial activity in the public domain, refer to <https://pharmaintelligence.informa.com/resources/product-content/clinical-trials-activity-analysis-factoring-in-delayed-reporting>.

2. Unapproved drugs have not received regulatory approval for any indication. This excludes drugs that were approved for an initial indication, but are unapproved for additional indications or other patient populations. Trials evaluating multiple drugs are classified as an unapproved drug trial if at least one primary drug is unapproved.

3. Trials that include multiple indications across different therapeutic areas will be counted for each targeted TA. As such, the sum of trial counts for the eight TAs will be higher than the total number of Phase I–III trials started in 2017.

4. Trial counts for infectious disease (ID) include activity from vaccines (infectious diseases), which is a separate TA module within Trialtrove. For the purposes of this analysis, all ID activity has been combined into a singular TA.

5. Lloyd I (2018) Pharma R&D Annual Review 2018. Available from: <https://pharmaintelligence.informa.com/resources/product-content/pharma-rd-annual-review-2018> [Accessed July 11, 2018].

6. Datamonitor Healthcare, July 2018.

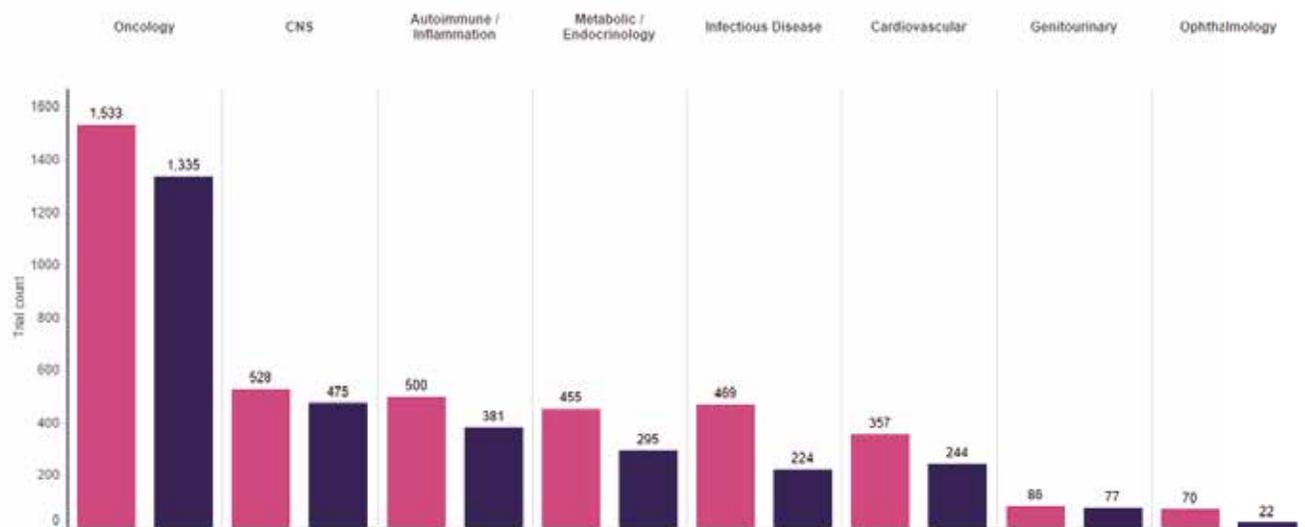
The only other TA that did not increase the level of trial initiations for 2017 was ophthalmology, which held nearly the same number of trial starts in 2017 and 2016 (Figure 1: Therapeutic areas by rank order). Trials with unapproved drugs continue to outnumber those focusing solely on approved drugs for all TAs. However, shifts in drug development strategy are observed for some TAs. 2016 trial starts revealed that the largest market expansion efforts were observed in oncology, CNS, and metabolic, and nearly half of these trials involved approved drugs alone. While the same is true for oncology and CNS with regard to their 2017 trial starts, the level of approved drug activity decreased for metabolic

trials. On the other hand, A/I and genitourinary ramped up their market expansion efforts to similar levels as oncology and CNS (see Figure 1: Distribution of trials by drug approval status).

The TAs with the highest percentage of unapproved drug activity include ophthalmology, which continued to have the starkest difference between approved and unapproved drug research, as well as ID. While activity had decreased for ID overall, the area remained focused in driving innovation for the sector (Figure 1: Distribution of trials by drug approval status).

Figure 1. Phase I–III clinical trials started in 2017, by drug status

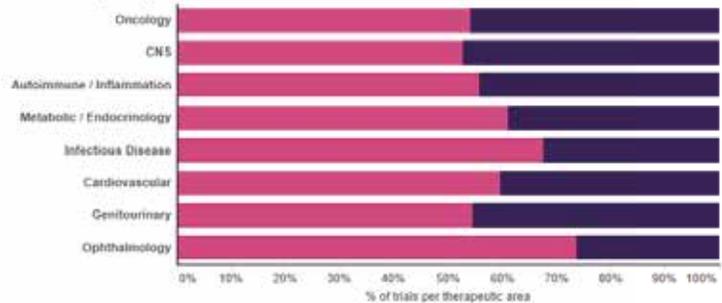
Therapeutic areas by rank order



Drug approval status



Distribution of trials by drug approval status

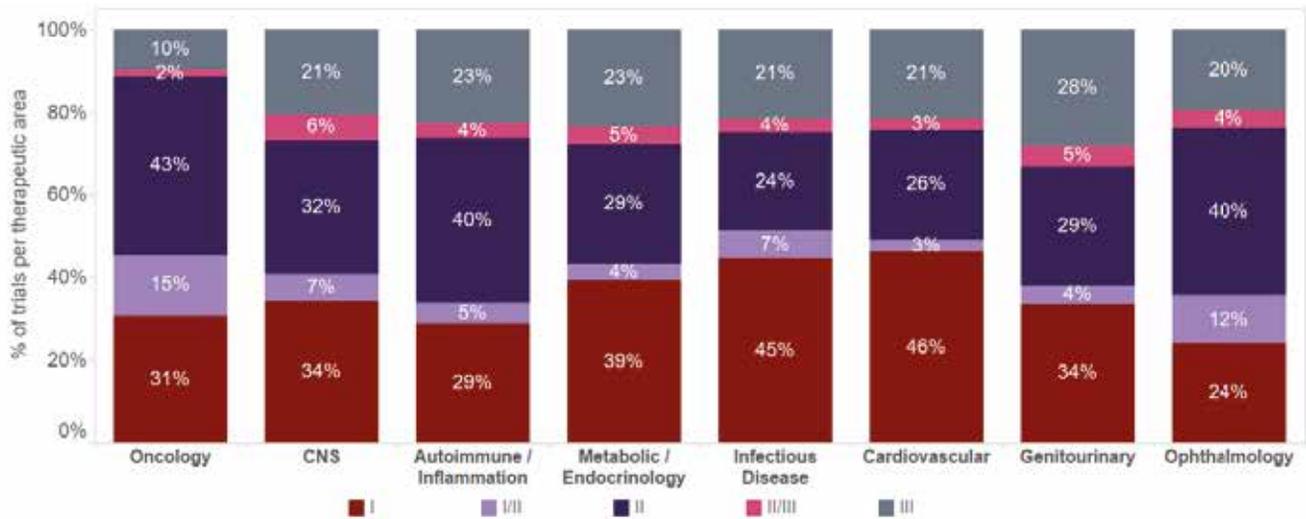


Powered by Informa's Trials API
Source: Trialstrove@ June 2018

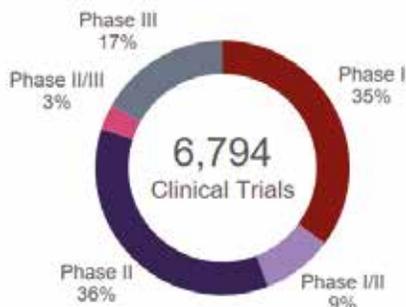
Oncology and A/I both continue to be largely driven by Phase II activity, followed by Phase I, however, CNS shifted its focus toward earlier-stage trials. While last year's analysis found that Phase II research was the most robust area for CNS in 2016, followed by Phase I, this flipped in 2017, and CNS had slightly more Phase I activity than Phase

II (34% versus 32%). Nearly all the remaining TAs also favored Phase I in their 2017 trial starts, except ophthalmology. Here, in another change from last year's analysis when Phase III activity led, 2017 held a larger number of Phase II starts within this small TA (Figure 2).

Figure 2. Distribution of Phase I–III clinical trials started in 2017, by phase



Overall



Trial counts by phase

	I	I/II	II	II/III	III	Total
Oncology	883	416	1,242	50	277	2,868
Metabolic / Endocrinology	294	31	217	34	174	750
Cardiovascular	278	18	158	18	129	601
CNS	342	68	325	60	208	1,003
Autoimmune / Inflammation	254	46	350	31	200	881
Genitourinary	55	7	47	8	46	163
Infectious Disease	309	46	165	25	148	693
Ophthalmology	22	11	37	4	18	92
Total	2,385	626	2,420	222	1,141	6,794

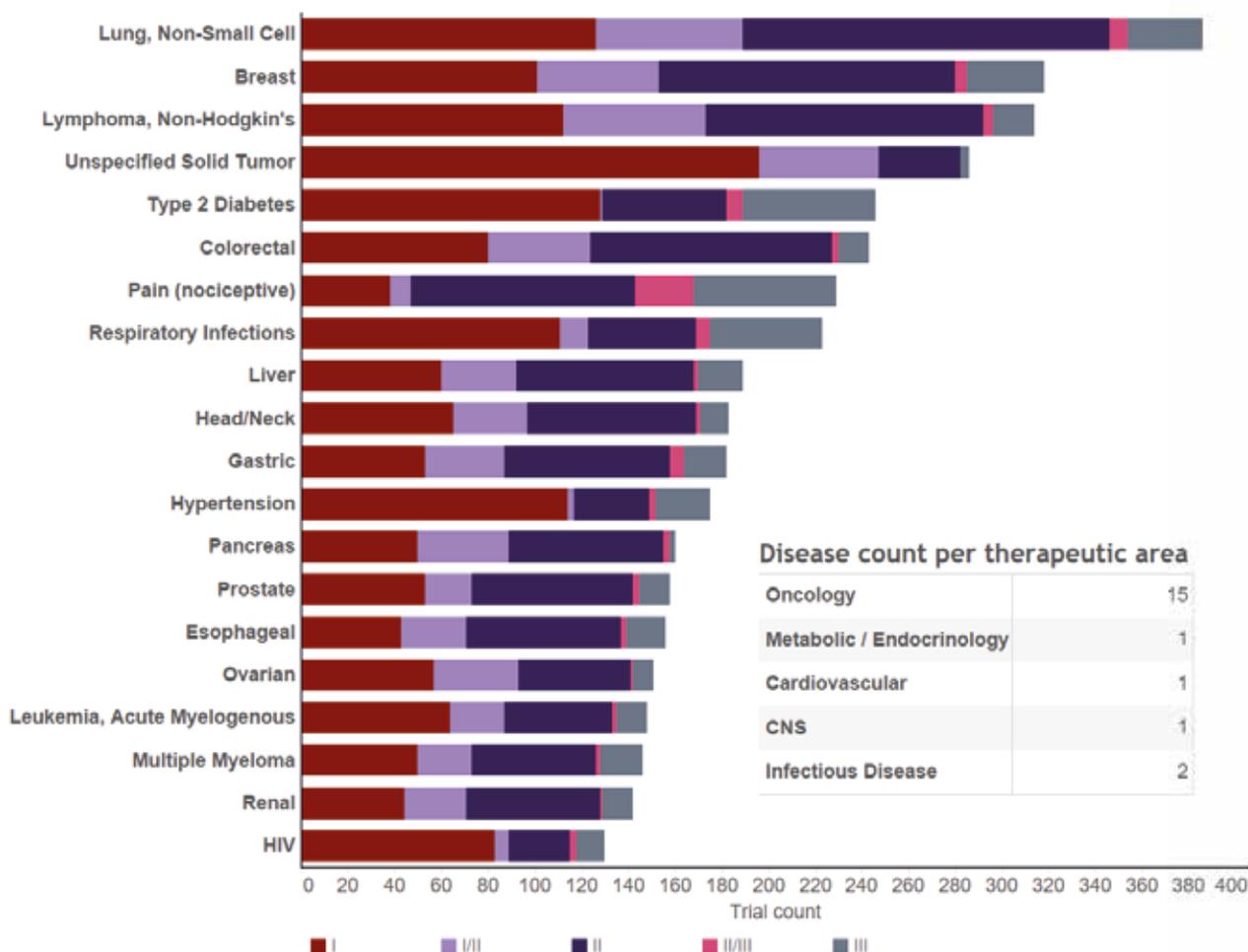
Powered by Informa's Trials API
Source: Trialtrove® June 2018

Among the Top 20 diseases in newly initiated trials in 2017, the fight against cancer takes top billing, and 15 of the Top 20 diseases were various cancers, including the four most active indications: non-small cell lung cancer (NSCLC), breast cancer, non-Hodgkin’s lymphoma (NHL), and unspecified solid tumor. Colorectal cancer was a close contender for fifth place, but type 2 diabetes (T2D) edged out this cancer with a difference of three trials. The remaining top non-oncology diseases include one each for CNS and cardiovascular, and two for ID, including HIV. Although multiple effective regimens are available to effectively treat patients, and overall activity has decreased for ID, HIV research remains active due to ongoing efforts with vaccines and immunomodulatory approaches that aim to either prevent or facilitate a cure when used in

combination with standard antiretroviral regimens (Figure 3). This year, no A/I diseases make the Top 20, although asthma falls just out of the picture at 23rd place.

Considering the bulk of oncology activity was in Phase II, and the Top 20 diseases primarily comprised various cancers, it follows that the majority had Phase II as the largest percentage of their disease-specific activity (13 diseases). The remaining seven displayed a larger proportion of Phase I trials. In terms of the top diseases for the individual phases, unspecified solid tumors continued to lead in the number of Phase I trials initiated in 2017, while NSCLC led Phase II, and T2D for Phase III (Figure 3).

Figure 3. Top 20 diseases for Phase I–III clinical trials started in 2017, by trial count



Powered by Informa’s Trials API
Source: Trialtrove® June 2018

The Leading Parents Behind the Trials

A sizable portion of new clinical research continues to be driven by a small cohort of companies – 23% of all Phase I–III trials included in this analysis were initiated by the Top 20 most active industry sponsors/collaborators, at a total of 1,575 trials.⁷ This year's analysis finds a new star with Bristol-Myers Squibb (BMS), which rose to the top from fifth place in last year's roundup, unseating the prior leading company, AstraZeneca. The bulk of BMS's activity was driven by ongoing efforts with Opdivo (nivolumab), which has been approved in nine tumor types and 15 indications, yet still continues to demonstrate potential for further growth. AstraZeneca was a close second, with Merck & Co, Roche, and Johnson & Johnson rounding out the top five (Figure 4).

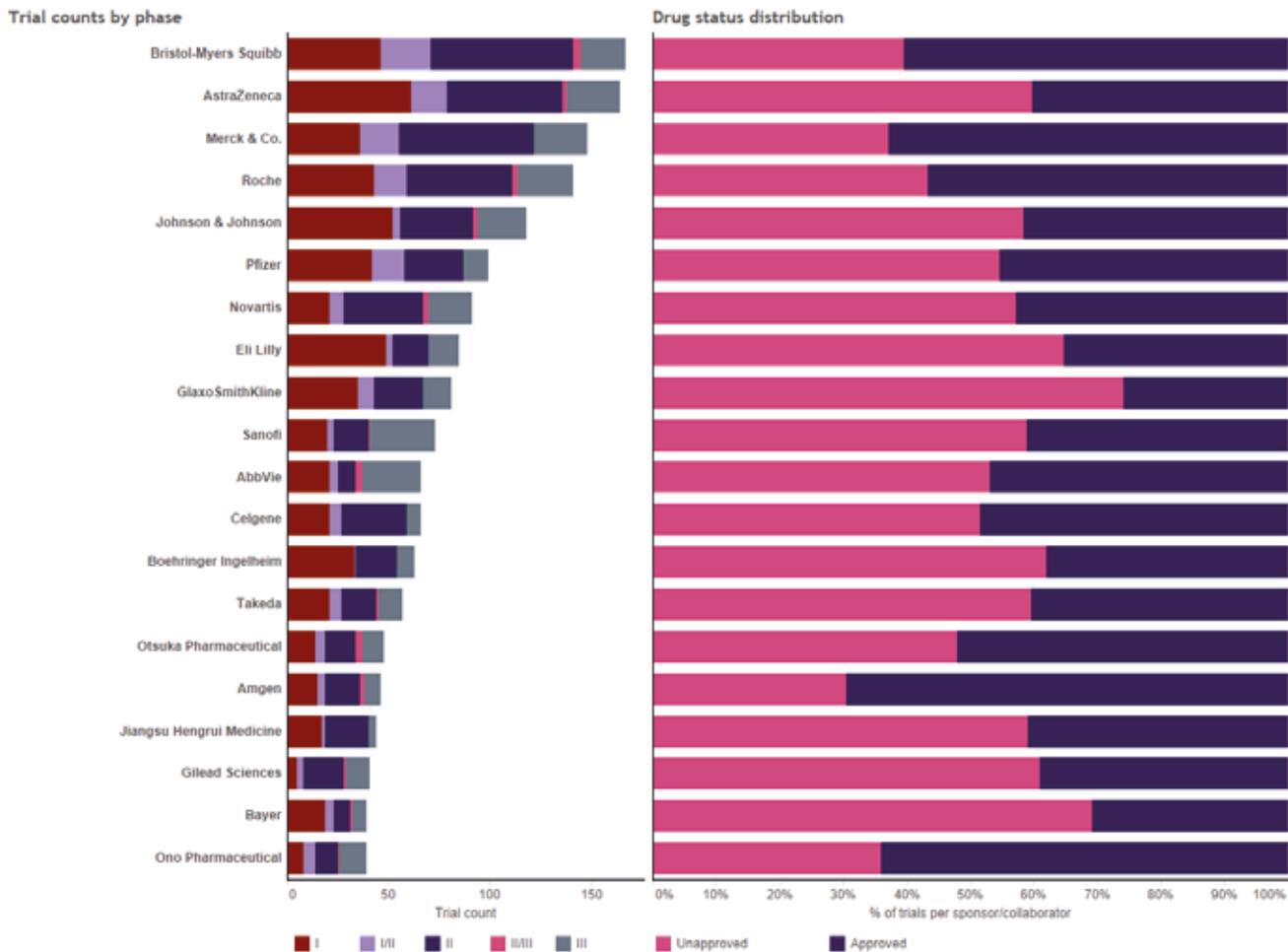
The majority of the roster includes repeat performances from prior roundups, with three cast replacements. While Novo Nordisk, Astellas, and Daiichi Sankyo have dropped out of the Top 20 for this year's analysis, Otsuka Pharmaceutical, Amgen, and Ono Pharmaceutical entered the stage (Figure 4). However, over half of Ono's activity was driven by its partnership with BMS (21/39 trials; 54%), primarily consisting of Opdivo trials. This collaboration was the most prolific among partnerships between two Top 20 companies in terms of the number of collaborative trials initiated in 2017. The second most active partnership was

between AstraZeneca and Eli Lilly, which initiated a total of three trials in collaboration. Two trials were to evaluate lanabecestat for Alzheimer's disease, including the recently discontinued global Phase III AMARANTH extension trial, while the third trial combined targeted therapies from each company to treat advanced solid tumors (data not shown). In addition to being the overall leader, BMS also started the largest number of Phase II trials in 2017, as well as Phase I/II, due to its focused efforts with Opdivo. The prior leader, AstraZeneca, held first place for the largest number of Phase I trials, while Sanofi started the largest number of Phase III trials. In fact, nearly half of Sanofi's 2017 trial starts were Phase III, unlike the majority of companies which primarily initiated early to mid-stage clinical trials (Figure 4: Trial counts by phase).

Unapproved drug trials were a larger focus for 14 companies from this cohort, with GlaxoSmithKline (GSK) leading as the company with the largest proportion of unapproved drug trials. For the remaining six companies prioritizing market expansion activities, Amgen had the largest proportion, with nearly 70% of 2017 trial starts evaluating approved drugs alone. AbbVie, Celgene, and Otsuka had near even proportions of approved and unapproved drug trial activity, balancing innovation with strategic use of well-established assets (Figure 4: Drug status distribution).

7. Similar to disease counts, the trial counts by sponsor represent each study that the sponsor was involved in, including collaborative research. Trials that include multiple sponsors will be counted for each company.

Figure 4. Top 20 industry sponsors/collaborators by number of Phase I–III trials started in 2017



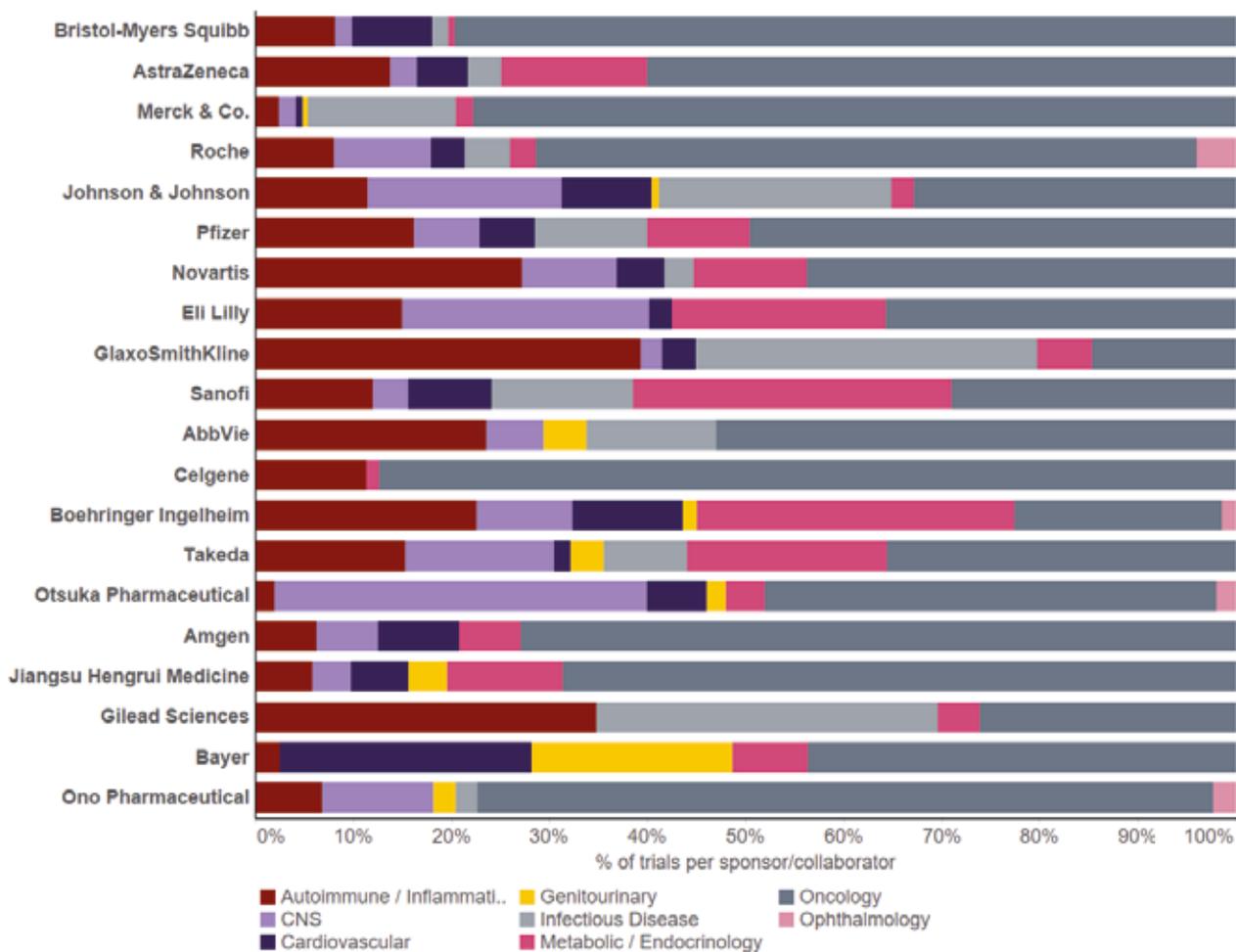
Powered by Informa's Trials API
Source: Trialtrove@ June 2018

Oncology also dominates when assessing the therapeutic focus of trials initiated in 2017 by the Top 20 companies – 16 had the largest proportion of their activity targeting cancer, including nine with percentages over 50%. Besides these companies, two had the most activity in metabolic (Sanofi and Boehringer Ingelheim), and GSK was the sole company with the largest percentage of 2017 activity being within A/I. While Gilead also prioritized A/I activity, the company evenly split its largest efforts between A/I and ID (Figure 5).

Most companies diversified efforts and started trials across six to seven TAs, albeit some initiated

limited activity for TAs outside their main focus area. For instance, oncology comprised approximately 80% of BMS's trials, while activity in five other TAs ranged from 1–8% of its trials. A few companies demonstrated larger allocations across multiple TAs, such as Takeda – while 36% of Takeda's 2017 trial starts were in oncology, the company also started 20% of its trials in metabolic, and 15% in A/I as well as CNS. Celgene demonstrated the largest therapeutic focus and concentrated 87% of its efforts into oncology trials, accompanied by small efforts in A/I and limited activity in metabolic (Figure 5).

Figure 5. Distribution of therapeutic areas for Top 20 sponsors/collaborators starting trials in 2017



Powered by Informa's Trials API
Source: Trialtrove® June 2018

Table 1 outlines the headliners within the individual TAs, where the Top 20 sponsors/collaborators dominated the most active TAs, particularly in oncology, while non-Top 20 companies continued to lead in the smaller areas of genitourinary and ophthalmology. Again BMS rises to the top for oncology, surpassing the trial activity of its key competitor, Merck. Novo Nordisk and Daiichi Sankyo, companies present as Top 20 sponsors/collaborators in last year's roundup, make appearances as top sponsors/collaborators for metabolic and cardiovascular, respectively.

Two newcomers include Galapagos for A/I and Lundbeck for CNS. Galapagos's activity included collaborative efforts with Gilead to assess filgotinib, a highly selective Janus kinase 1 (JAK1) inhibitor, for indications such as Crohn's disease, ulcerative colitis, and various types of arthritis. Lundbeck's activity was also supported by a Top 20 partner, Otsuka, through their joint efforts on evaluating Rexulti (brexiprazole) in multiple trials for schizophrenia and bipolar disorders, as well as for post-traumatic stress disorder and in pediatric populations (Table 1).

Table 1. Top sponsors per therapeutic area for Phase I–III clinical trials starting in 2017

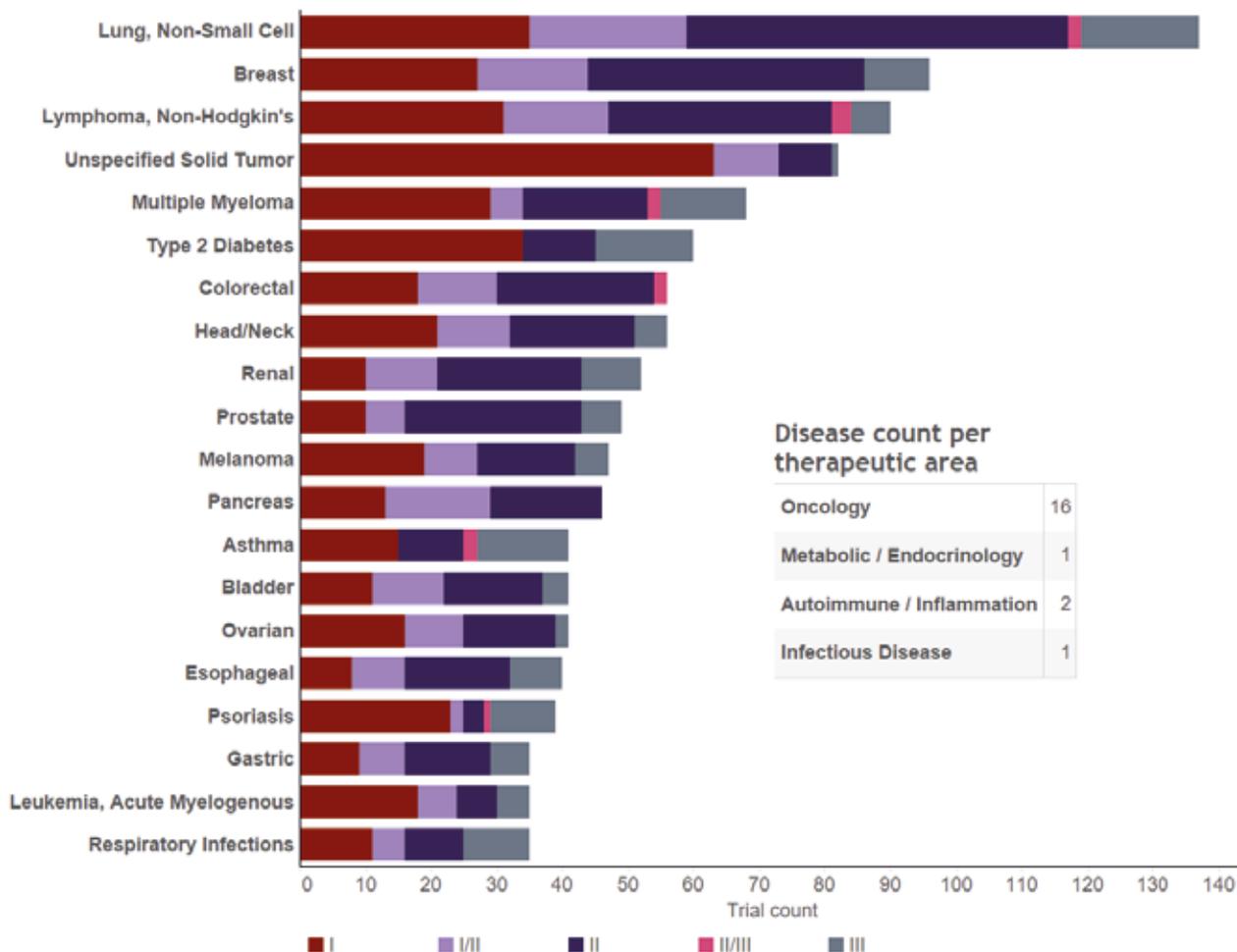
Autoimmune/ Inflammation (n = 881)		Cardiovascular (n = 601)		CNS (n = 1,003)		Genitourinary (n = 163)	
Sponsor	Trials	Sponsor	Trials	Sponsor	Trials	Sponsor	Trials
GlaxoSmithKline	35	Bristol-Myers Squibb	14	Johnson & Johnson	25	Bayer	8
Novartis	25	Johnson & Johnson	12	Eli Lilly	22	Roivant Sciences	7
AstraZeneca	23	Bayer	10	Otsuka Pharmaceutical	19	AbbVie	3
Galapagos	21	AstraZeneca	9	Lundbeck	16	Ferring	3
Pfizer	17	Boehringer Ingelheim	8	Roche	15	ObsEva	3
		Daiichi Sankyo	8			Qilu Pharmaceutical Co.	3
Infectious Disease (n = 693)		Metabolic/Endocrinology (n = 750)		Oncology (n = 2,868)		Ophthalmology (n = 92)	
Sponsor	Trials	Sponsor	Trials	Sponsor	Trials	Sponsor	Trials
Johnson & Johnson	25	Novo Nordisk	29	Bristol-Myers Squibb	133	Senju	6
GlaxoSmithKline	23	Sanofi	27	Merck & Co.	123	Roche	5
Gilead Sciences	16	AstraZeneca	24	AstraZeneca	103	Aerie Pharmaceuticals	3
Merck & Co.	16	Boehringer Ingelheim	22	Roche	98	Laboratorios Sophia	3
ViiV Healthcare	10	Eli Lilly	19	Celgene	60	Rocket Pharmaceutical	3
						Santen	3

Powered by Informa's Trials API
Source: Trialtrive® June 2018

Turning back to the Top 20 sponsors/collaborators and the diseases targeted by this cohort, most were in line with the diseases popular across all trials initiated in 2017. A few indications were key priorities for these prolific companies, but not for the overall cohort, specifically melanoma, bladder cancer, asthma, and psoriasis, which replaced nociceptive pain, liver cancer, hypertension, and HIV. In line with the strong oncology focus observed for the Top 20 sponsors, 16 of the most active diseases were cancers, again led by NSCLC, breast cancer, NHL, and unspecified solid tumor, with multiple myeloma taking fifth place (Figure 6).

In terms of the preferred phase of development, Phase I and II shared the largest number of trials, with 10 diseases each. However, there was only a single trial difference between Phase I/II and II for pancreatic cancer, and between Phase I and III for both asthma and respiratory infections, with Phase II closely following for the latter. In contrast to last year when HCV was the sole indication with the bulk of activity in Phase III, no diseases this year had late-stage research as their most robust area (Figure 6).

Figure 6. Top diseases for trials started in 2017 by the most active industry sponsors/collaborators



Powered by Informa's Trials API
Source: Trialtrive@ June 2018

Table 2 provides an overview of the diseases with the largest number of 2017 trial starts for each company. A total of 42 diseases were targeted by the Top 20 sponsors/collaborators, four of which included various cancers as the focus for their top diseases. The most popular indication was NSCLC, which was a priority for 10 companies and also the biggest area for the top three sponsors – BMS, AstraZeneca, and Merck. The combined NSCLC activity from these three companies alone comprised nearly 20% of all NSCLC trials initiated in 2017 (Table 2).

Other common indications included breast cancer, NHL, and unspecified solid tumor, each targeted by six companies. T2D was the most popular non-oncology indication, and the leading disease for Eli Lilly and Sanofi, whose combined efforts accounted for approximately 14% of all new T2D activity in 2017 (Table 2).

A number of indications were a unique priority, and 23 were a top disease for a single company within this cohort. Amgen and Takeda have the largest number of unique top diseases – gastroparesis, Crohn's disease, and gastroesophageal reflux disease (GERD) for Takeda; melanoma, dyslipidemia, and acute lymphocytic leukemia for Amgen. Other unique priorities include HIV for Gilead, despite the previously mentioned fact that the company has saturated the market with various STRs, including its new flagship product, Biktarvy, consisting of bictegravir, emtricitabine, and tenofovir alafenamide. While the majority of Gilead's HIV activity evaluates established antiretrovirals in switch studies or as prophylactic interventions, the company is venturing outside of traditional HIV treatments with a Phase I trial of vesatolimod, an oral toll-like receptor 7 agonist that activates both innate and adaptive immune responses (Table 2).

Table 2. Top diseases by sponsor/collaborator for clinical trials starting in 2017

Bristol-Myers Squibb	Lung, Non-Small Cell (31)	Head/Neck (16)	Renal (14)
AstraZeneca	Lung, Non-Small Cell (24)	Ovarian (13) Unspecified Solid Tumor (13)	Asthma (11) Chronic Obstructive Pulmonary Disease (11) Type 2 Diabetes (11)
Merck & Co.	Breast (20) Lung, Non-Small Cell (20)	Unspecified Solid Tumor (14)	Esophageal (11)
Roche	Breast (19)	Lymphoma, Non-Hodgkin's (18)	Lung, Non-Small Cell (13)
Johnson & Johnson	Multiple Myeloma (15)	Prostate (14)	Depression (13)
Pfizer	Breast (10) Lung, Non-Small Cell (10)	NAFLD (7) Prostate (7) Renal (7)	Ulcerative Colitis (6) Unspecified Solid Tumor (6)
Novartis	Asthma (11)	Breast (10)	Lung, Non-Small Cell (6) Obesity (6)
Eli Lilly	Type 2 Diabetes (15)	Migraine (13)	Alzheimer's Disease (6) Psoriasis (6) Type 1 Diabetes (6)
GlaxoSmithKline	Asthma (12)	Chronic Obstructive Pulmonary Disease (10)	Respiratory Infections (7)
Sanofi	Type 2 Diabetes (19)	Type 1 Diabetes (8)	Prostate (5)
AbbVie	Lymphoma, Non-Hodgkin's (10)	HCV (9)	Psoriasis (6)
Celgene	Multiple Myeloma (18)	Lymphoma, Non-Hodgkin's (11)	Leukemia, Acute Myelogenous (5) Lung, Non-Small Cell (5)
Boehringer Ingelheim	Diabetic Complications (10) Lung, Non-Small Cell (10) Renal Disease (10)	Type 2 Diabetes (8)	Psoriasis (6)
Takeda	Gastroparesis (6) Schizophrenia (6)	Chrohn's Disease (5) Lymphoma, Non-Hodgkin's (5)	GERD (4) Ulcerative Colitis (4) Unspecified Solid Tumor (4)
Otsuka Pharmaceutical	Schizophrenia (6)	Lung, Non-Small Cell (5)	Bipolar Disorder (4) Colorectal (4) Leukemia, Acute Myelogenous (4)
Amgen	Multiple Myeloma (10)	Colorectal (4) Lymphoma, Non-Hodgkin's (4) Melanoma (4)	Breast (3) Dyslipidemia (3) Leukemia, Acute Lymphocytic (3)
Jiangsu Hengrui Medicine	Esophageal (6)	Lung, Non-Small Cell (4) Unspecified Solid Tumor (4)	Colorectal (3) Gastric (3) Hyperuricemia/Gout (3) Liver (3)
Gilead Sciences	HCV (7)	HIV (5)	Lymphoma, Non-Hodgkin's (4)
Bayer	Prostate (6)	Congestive Heart Failure (5)	Breast (4) Uterine Fibroids (4)
Ono Pharmaceutical	Lung, Non-Small Cell (9)	Unspecified Solid Tumor (5)	Esophageal (4) Gastric (4) Pain (nociceptive) (4)

*Top diseases limited to indications with at least 3 or more trials

Powered by Informa's Trials API
Source: Trialstrove® June 2018

Investments Behind the Scenes

Clinical trials are a costly endeavor, and account for a large proportion of companies' R&D budgets. On average, \$5.5bn was invested into R&D by the Top 20 sponsors in 2017. Although R&D spend does fund activities outside of clinical research, such as discovery and preclinical drug development, we sought to approximate the usage of each company's R&D investment by comparing the 2017 R&D spend⁸ with the total number of trials started in 2017, as well as the number of currently ongoing trials.⁹

The largest investment was made by Roche, which was fourth in terms of 2017 trial starts, and had an R&D spend of nearly \$12.8bn in 2017. In addition to the large volume of new trials, the high investment also supports significant ongoing research, as Roche also holds the largest number of ongoing Phase I–III trials as of June 2018. Roche was followed by J&J, which spent approximately \$10.6bn, with lower levels of activity for both 2017 trial initiations and ongoing research. On the other end of the spectrum, Jiangsu Hengrui was the lowest spender, although the company did increase its R&D investments over

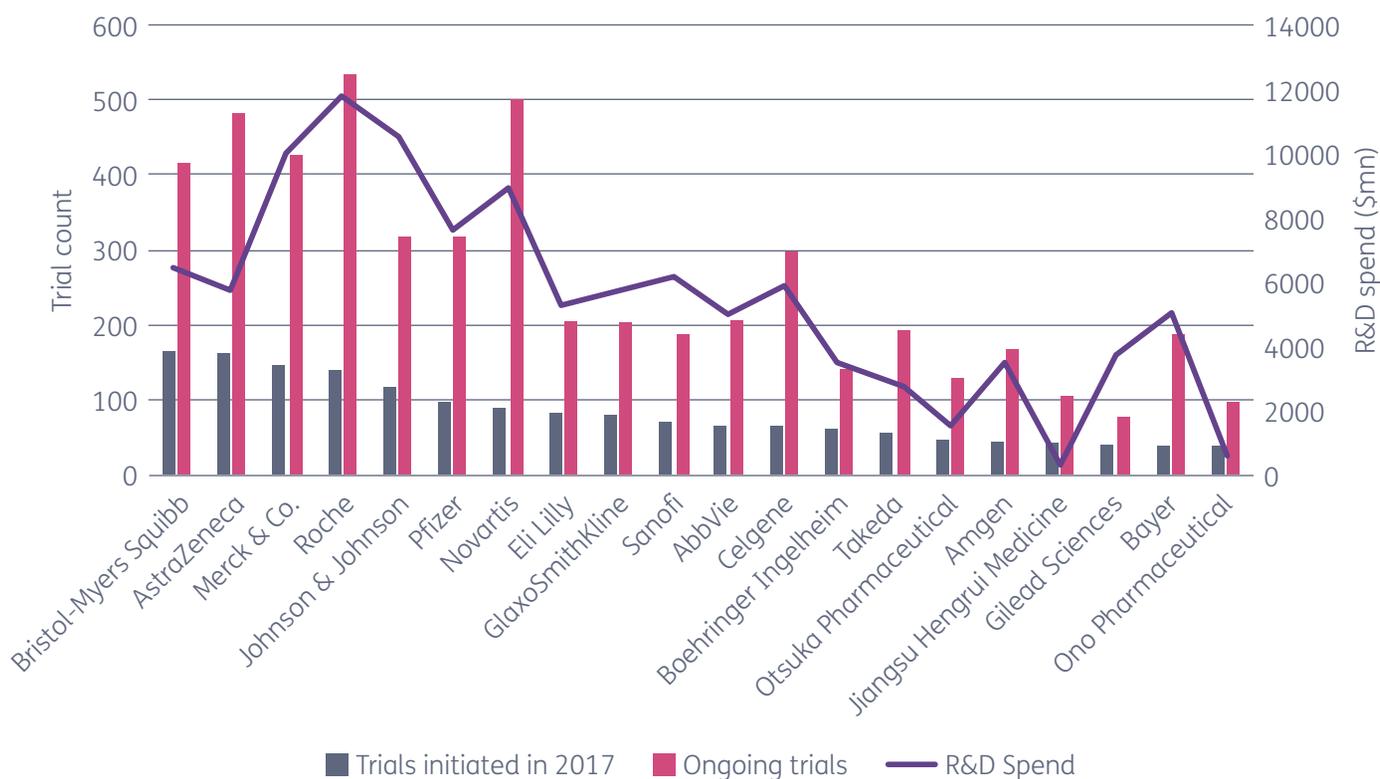
the prior year, as well as trial activity (Figure 7).

These companies demonstrate varying levels of value potentially derived from the significant investments made into R&D. For instance, despite the larger volume of ongoing trials, and comparable number of trial initiations in 2017, AstraZeneca maintains a lower spend than the new leader of the roundup, BMS. Amgen and Bayer also initiated a similar volume of trials in 2017, yet the difference in their R&D spend seems to be reflected in the level of ongoing activity, with Bayer spending more and supporting more ongoing trials than Amgen. However, R&D spend does not appear to be directly correlated with ongoing trial activity for other companies, as the converse is true for J&J and Pfizer. While these two companies possess comparable ongoing activity, J&J outspends Pfizer after initiating more trials in 2017 (Figure 7). These differences could be attributed in part to the complexity of protocols for individual trials, among other contributing factors outside of sheer trial volume.

8. R&D expenditures from the calendar year of 2017 are included in the analysis, and are reported in US dollars. Due to the differing fiscal year in Japan, the R&D spend for Japan-based companies is the sum of Q4 FY2016 and Q1 to Q3 FY2017. Currency conversions are based on the average exchange rates for 2017.

9. Includes Phase I–III trials, regardless of start date, that were ongoing in Trialrove as of June 14, 2018.

Figure 7. Phase I–III trials initiated in 2017 and total ongoing trials relative to R&D spend*



*Reflects R&D spend in the calendar year of 2016. Currency conversions, when applied, are based on the average exchange rate for 2016.

Source: Company filings; Trialtrove® June 2018

In terms of how these companies are maximizing the use of their drug pipelines, overall, this cohort averages 2.1 ongoing trials for each of their drugs in active clinical development. Novartis possesses the largest portfolio of active drugs, fueling its large volume of ongoing trials, and holds a slightly higher ratio of 2.3. However, the highest ratio of trials per drug falls to Jiangsu, which has 4.8 ongoing trials for each of its active drugs, maximizing activity for its small pipeline. Sanofi and GSK have the lowest trial densities, with approximately 1 trial per each active

drug, opting for a more diversified approach with their ongoing research (Table 3).

Among the most active sponsors/collaborators, BMS has the largest ratio, with 3.0 ongoing trials per drug. AstraZeneca has a lower ratio of 2.4, due to the larger pipeline of active drugs to evaluate across its larger number of ongoing trials. Merck’s ratio is comparable at 2.3, but J&J has the lowest ratio among the top five, with 1.5 (Table 3).

Table 3. Ratio of ongoing Phase I–III trials to drugs in active clinical development

Sponsor/Collaborator*	Active drugs	Ongoing trials	# of trials per drug
Bristol-Myers Squibb	137	417	3.0
AstraZeneca	198	483	2.4
Merck & Co.	182	427	2.3
Roche	195	536	2.7
Johnson & Johnson	218	319	1.5
Pfizer	179	319	1.8
Novartis	221	500	2.3
Eli Lilly	120	206	1.7
GlaxoSmithKline	183	205	1.1
Sanofi	191	188	1.0
AbbVie	93	207	2.2
Celgene	98	299	3.1
Boehringer Ingelheim	94	142	1.5
Takeda	167	194	1.2
Otsuka Pharmaceutical	91	130	1.4
Amgen	89	169	1.9
Jiangsu Hengrui Medicine	22	106	4.8
Gilead Sciences	71	118	1.7
Bayer	119	189	1.6
Ono Pharmaceutical	43	98	2.3

*Sponsors/collaborators limited to Top 20 companies initiating the largest number of trials in 2017.

Source: Pharmaprojects®, Trialtrive® June 2018

Thriving Environments for the 2017 Clinical Trials

The lion’s share of trials initiated in 2017 continues to include the US as a location, followed by China, consistent with last year’s roundup. The number of trials increased for both countries, however, and China saw a significant increase in activity in comparison to last year’s analysis. While 845 trials initiated in 2016 included China as a location, the volume ramped up to 1,252 new trials in 2017. Also of note, China is the top location for cardiovascular trials, driven by activity within hypertension, thrombotic disorders, coronary artery disease, and dyslipidemia, when typically the US holds the number one spot across all TAs, as well as overall (Table 4).

Besides the US and China, the top 10 countries across all newly initiated trials in 2017 spans typical

markets, such as the UK, Germany, Japan, Spain, Canada, and France. In last year’s analysis, Russia and South Korea were also included as key markets, but were replaced by Australia and Italy when assessing 2017 activity (Table 4).

Similar regions are targeted when limiting the view to specific TAs, but South Korea does make an appearance for five. Russia is only included for two TAs, indicating prioritization of other markets for most TAs, such as Poland, which was a top location for A/I, cardiovascular, CNS, and genitourinary. Australia’s inclusion within the overall top locations for 2017 research appears to be driven by the robust oncology activity taking place in the country, as well as other TAs such as A/I, CNS, and ID (Table 4).

Table 4. Top locations for Phase I–III trials starting in 2017, by therapeutic area

Overall	
Country	Trials
United States	2746
China	1252
United Kingdom	657
Germany	621
Japan	588
Spain	537
Canada	528
France	492
Australia	428
Italy	413

Autoimmune/ Inflammation	
Country	Trials
United States	327
United Kingdom	147
Germany	146
Canada	114
China	110
Poland	99
Spain	97
Australia	91
Japan	86
France	83

Cardiovascular	
Country	Trials
China	170
United States	155
Germany	67
United Kingdom	67
Canada	49
Spain	49
Netherlands	46
South Korea	40
Japan	39
Italy	36
Poland	36

CNS	
Country	Trials
United States	435
China	98
United Kingdom	95
Germany	79
Spain	70
Canada	69
Japan	64
Australia	58
France	58
Poland	55

Genitourinary	
Country	Trials
United States	41
China	24
Iran	17
Poland	12
Egypt	10
Germany	10
India	10
Russia	10
Czech Republic	9
Italy	9
Spain	9

Infectious Disease	
Country	Trials
United States	219
China	144
United Kingdom	60
Canada	46
Russia	43
France	42
Spain	42
Germany	38
Australia	33
South Korea	32

Metabolic/Endocrinology	
Country	Trials
United States	248
China	99
Germany	79
Canada	69
United Kingdom	62
Japan	61
Iran	56
India	54
Italy	44
South Korea	44

Oncology	
Country	Trials
United States	1375
China	623
Japan	313
France	251
Spain	250
United Kingdom	242
Germany	222
Australia	192
Canada	191
South Korea	191

Ophthalmology	
Country	Trials
United States	40
Japan	15
China	7
Spain	7
United Kingdom	7
Italy	6
Australia	5
South Korea	5
France	4
Germany	4

Powered by Informa's Trials API
Source: Trialstrove® June 2018

The US was the most popular location across the more active sponsors/collaborators, but each company's second choice varied widely. Most targeted major markets such as the UK, Germany, France, or Japan after the US, except for Pfizer, which had a second most frequented clinical trial destination of Belgium, followed by Canada (Table 5).

The Asia-Pacific (APAC) market was a common target for the majority of the companies included in Table 5. The outlier was Sanofi, which opted to focus on the emerging markets in Eastern Europe, including Poland, Hungary, and Russia. As for APAC, Australia and Japan were included as a top location for six companies each, with Japan being a second-choice destination for Eli Lilly in 2017 trial starts. Eli Lilly also opted for the unique target of Singapore.

While China is consistently a top location overall for newly initiated trials, this activity is primarily driven by China-based companies, and the country drops out as a top location for the most active industry sponsors/collaborators due to regulatory considerations. As such, it is noteworthy to see China as a top destination for AstraZeneca, demonstrating the company's longstanding commitment to the country, which is finally being reflected in the volume of new trial activity (Table 5). As a further demonstration of this commitment, AstraZeneca announced a strategic joint venture with the Chinese Future Industry Investment Fund toward the end of 2017, to form an equally owned, standalone company based in China to bring innovative new medicines to patients in China faster, as well as globally.¹⁰

Table 5. Top locations for trials starting in 2017 by most active industry sponsors/collaborators*

Bristol-Myers Squibb		AstraZeneca		Merck & Co.		Roche		Johnson & Johnson	
Country	Trials	Country	Trials	Country	Trials	Country	Trials	Country	Trials
United States	121	United States	85	United States	104	United States	94	United States	64
France	31	United Kingdom	38	United Kingdom	31	Germany	43	Germany	29
Japan	28	Germany	26	France	26	Spain	42	Belgium	27
Germany	27	South Korea	26	Canada	24	United Kingdom	36	Spain	27
Spain	26	France	25	Spain	24	Canada	35	France	24
Canada	25	Japan	23	Australia	20	Australia	32	Poland	22
Australia	24	Canada	19	Germany	20	France	30	Canada	19
United Kingdom	23	Spain	18	Japan	18	South Korea	28	Czech Republic	19
Italy	21	China	15	South Korea	18	Belgium	27	Australia	17
Netherlands	20	Russia	15	Italy	17	Italy	27	Russia	15
								United Kingdom	15

Pfizer		Novartis		Eli Lilly		GlaxoSmithKline		Sanofi	
Country	Trials	Country	Trials	Country	Trials	Country	Trials	Country	Trials
United States	68	United States	62	United States	49	United States	41	United States	43
Belgium	19	Germany	38	Japan	21	United Kingdom	26	United Kingdom	21
Canada	14	Spain	32	Germany	19	Germany	17	Germany	20
Spain	12	Canada	30	Canada	13	Canada	16	France	19
France	11	United Kingdom	30	Spain	12	Spain	12	Italy	19
Australia	10	France	27	United Kingdom	11	Russia	11	Spain	19
Germany	10	Netherlands	27	Italy	10	Australia	10	Canada	17
United Kingdom	10	Italy	26	Argentina	9	Romania	9	Poland	17
Poland	9	Belgium	24	France	9	South Korea	8	Hungary	14
Czech Republic	8	Japan	24	Hungary	9	France	7	Russia	13
				Mexico	9	Italy	7		
				Poland	9	Japan	7		
				Singapore	9				

*Sponsors/collaborators limited to top 10 companies initiating the largest number of trials in 2017.

Powered by Informa's Trials API
Source: Trialtrove® June 2018

10. AstraZeneca (2017) AstraZeneca and Chinese Future Industry Investment Fund establish joint venture to develop new medicines in China. Available from: <https://www.astrazeneca.com/media-centre/press-releases/2017/astrazeneca-and-chinese-future-industry-investment-fund-establish-joint-venture-to-develop-new-medicines-in-china-27112017.html> [Accessed July 18, 2018].

Moving back to the entire cohort of the Top 20 companies, an overall average of 4.6 countries were disclosed per trial, which ranged from Jiangsu Hengrui Medicine's 1.0 to AbbVie's 9.9. AbbVie's large average number of countries used per trial is due to the size of its Phase III trials value (18.2). However, the largest Phase III trials by average geographic breadth goes to Novartis, with a slightly higher average of 18.8 (Table 6).

Novartis also opted to include more countries, on average, to recruit for its Phase I trials. While an overall mean of 1.6 countries were used in this cohort's Phase I trials, Novartis averaged 4.6 countries for each Phase I trial started by the company in 2017. Novartis's Phase II trials were also on the larger side, using 5.5 countries while the

entire cohort averaged 2.9, however, Bayer had a larger geographic breadth for its Phase II research of 6.2 countries per trial (Table 6).

Although some companies opted to include more countries to support recruitment for their trials, others demonstrated a more honed approach and focused efforts in limited markets. Besides Jiangsu Hengrui, which consistently used a single country in its trials regardless of phase, Otsuka Pharmaceutical runs the second smallest trials. Otsuka's Phase I and II trials are mostly single-country studies, primarily taking place in Japan and the US, while Phase III is slightly larger at 3.9 countries per trial on average. These multi-country trials expand beyond Japan and the US to include European and other Asian countries, as well as Canada (Table 6).

Table 6. Average number of countries disclosed per trial across the most active industry sponsors/ collaborators*

Sponsor	Average Number of Countries/Trial			
	Overall	I	II	III
Bristol-Myers Squibb	3.5	1.1	2.4	11.9
AstraZeneca	3.2	1.4	1.6	11.3
Merck & Co.	3.6	1.5	1.6	13.3
Roche	5.6	2.4	3.1	15.8
Johnson & Johnson	4.6	1.4	4.1	11.9
Pfizer	2.7	1.2	3.2	6.3
Novartis	8.8	4.6	5.5	18.8
Eli Lilly	3.6	1.2	2.0	13.9
GlaxoSmithKline	3.0	1.0	3.6	6.4
Sanofi	6.1	1.4	3.5	10.6
AbbVie	9.9	2.1	2.2	18.2
Celgene	3.4	1.2	3.1	11.7
Boehringer Ingelheim	4.2	1.5	3.2	16.2
Takeda	3.5	1.3	2.7	8.4
Otsuka Pharmaceutical	1.9	1.1	1.1	3.9
Amgen	3.9	2.5	2.1	10.0
Jiangsu Hengrui Medicine	1.0	1.0	1.0	1.0
Gilead Sciences	8.6	1.2	5.1	17.6
Bayer	4.4	1.9	6.2	7.6
Ono Pharmaceutical	6.0	1.0	1.7	14.0

*Excludes trials with no disclosed locations. Trial hybrids rolled into calculations for higher phase of development (i.e. Phase I/II included in Phase II calculations).

Powered by Informa's Trials API
Source: Trialstrove® June 2018

Concluding Thoughts

While trends such as oncology's dominance remain steadfast, the industry continues to evolve with new leading sponsors/collaborators, shifts in drug development strategies, and the emergence of (or declined activity in) key markets. Overall, activity is still tipped toward innovation, despite the risks and high costs involved. This is particularly true for the

small area of ophthalmology, as well as the recently shrinking area of ID. Hopefully this reduction in new ID trials is only temporary, and the innovation around unapproved drug research fuels further activity to address the numerous unmet needs, outside of the well-established markets of HIV and HCV, within the TA.

About the Author

Doro Shin, MPH
Director, Content Marketing

As a recognized thought leader, Doro heads the content marketing strategy and development for the Pharma Intelligence business at Informa. Drawing on nearly 15 years of experience supporting drug development, primarily as an Infectious and Genitourinary Disease analyst, for Citeline, Doro is acutely aware of the trends in the ever-changing pharmaceutical research landscape. As an analyst, Doro supported the editorial content of Citeline's pharmaceutical clinical trial products and assisted clients with competitive intelligence needs. Prior to Informa, Doro coordinated biomedical HIV prevention trials in Zimbabwe with the Women's Global Health Imperative at University of California, San Francisco (UCSF), and received her Master's degree in Public Health, with a specialty in Infectious Diseases, from the University of California, Berkeley.

pharma@informa.com

United States

605 Third Avenue
Floor 20-22
New York
NY 10158
USA
+1 908 547 2200
+1 888 670 8900

United Kingdom

Christchurch Court
10-15 Newgate Street
London
EC1A 7HD
United Kingdom
+44 20 337 73737

Japan

Shin-Kokusai Building,
4th Floor
3-4-1 Marunouchi
Chiyoda-ku
Tokyo
100-0005
+81 3 6273 4260

China

23rd Floor
16F Nexxus Building
41 Connaught Road
Hong Kong
China
+85 239 667 222

Australia

Level 18
347 Kent Street
Sydney
NSW 2000
+61 2 8705 6907

Informa's Pharma intelligence is home of the world's leading pharma and healthcare R&D and business intelligence brands – Datamonitor Healthcare, Sitetrove, Trialtrove, Pharmaprojects, Medtrack, Biomedtracker, Scrip, Pink Sheet, In Vivo. Pharma intelligence's brands are trusted to provide over 3000 of the world's leading pharmaceutical, contract research organizations (CRO's), medical technology, biotechnology and healthcare service providers, including the top 10 global pharma and top 10 CRO's, with an advantage when making critical R&D and commercial decisions.

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.

Pharma Intelligence © 2018.
All rights reserved. Pharma Intelligence is a trading division of Informa UK Ltd. Registered office: Mortimer House, 37-41 Mortimer Street, London W1T3JH, UK. Registered in England and Wales No 1072954

