



SYNERGY
ORANGE
PAPER

RESEARCH REPORT

CLINICAL TRIALS IN USA

ANNUAL 2018

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FOREWORD

The Orange Paper is a free publication produced by Synergy Research Group for the pharmaceutical industry since 2007. It pulls together data from numerous public sources into a single brief document to aid decision makers planning to conduct clinical trials. It is produced quarterly, with an annual summary at the close of each year.



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EXECUTIVE SUMMARY

During the year 2018 the official FDA website showed approvals for initiation of 25,186 new clinical trials of all types Worldwide, including local and bioequivalence studies. The number of studies initiated in the USA remained steady at 8,662 – a 0,5% increase in comparison with 2018.

The dominant type of clinical trials conducted in the year 2018 were Interventional Clinical Trials with 80% market share Worldwide and 88% market share in the USA. The most prevalent phase of clinical trials conducted Worldwide by number of studies is Phase II.

The total number of patients enrolled in Clinical trials of all types in the year 2018 exceeded 2 mln. people. The most prevalent Therapeutic areas of Clinical trials are Oncology and Cardiology.

During the year 2018 the Center for Drug Evaluation and Research (CDER) of the FDA approved 132 new drugs, including new molecular entities (NME), new dosages, combinations or manufacturers.

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) evaluated 78 new drugs, including 16 generics and 6 biosimilar drugs. Eight drugs were withdrawn, while 70 drugs received positive opinions and were approved to marketing.

According to the FDA data, 300 FDA inspections were conducted in the U.S. investigative sites (about 2/3 of them were conducted in the 1st half of the year) and 38 FDA inspections were conducted in investigative sites located in leading European countries during 2018. Countries which received the most inspections were Poland (9 inspections), Germany (6 inspections) and France (5 inspections).

The top tech trends in the Pharmaceuticals industry during 2018 were:

- Improving quality of Patient Relationship with patient-faced services like Medication Adherence apps, AI-based Diagnostic apps and Telemedicine services;
- Improving quality, speed and cost-efficiency in Clinical trials with Patient Engagement services, Remote Monitoring tools, Clinical Decision Support systems and In-Silico Drug Discovery approach;
- Improving speed and cost-efficiency in Clinical Practice of Healthcare Providers with AI-powered automated Diagnostic tools and voice-powered Physician's Assistant tools.





WORLDWIDE CLINICAL TRIALS

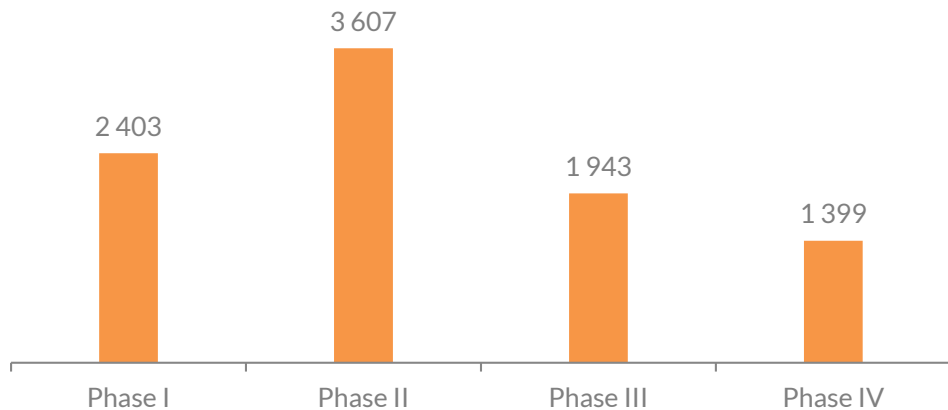
Trial Data

During the year 2018 the official FDA website showed approvals for initiation of 25,186 new clinical trials of all types worldwide, including local and bioequivalence studies with an overall year on year growth rate of 15% driven in large by an increasing number of trials in developing countries.

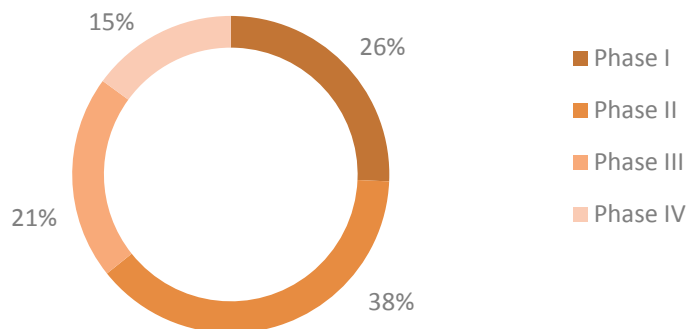
The combined market share of USA and European countries by number of initiated studies reached 71% in 2018, with the USA having 34% and Europe having 37%.

80% of all clinical trials initiated in 2018 were Interventional Clinical Trials.

Breakdown of Worldwide Clinical Trials by Phase in 2018



Percentage Breakdown of Clinical Trials by Phase in 2018 (worldwide)

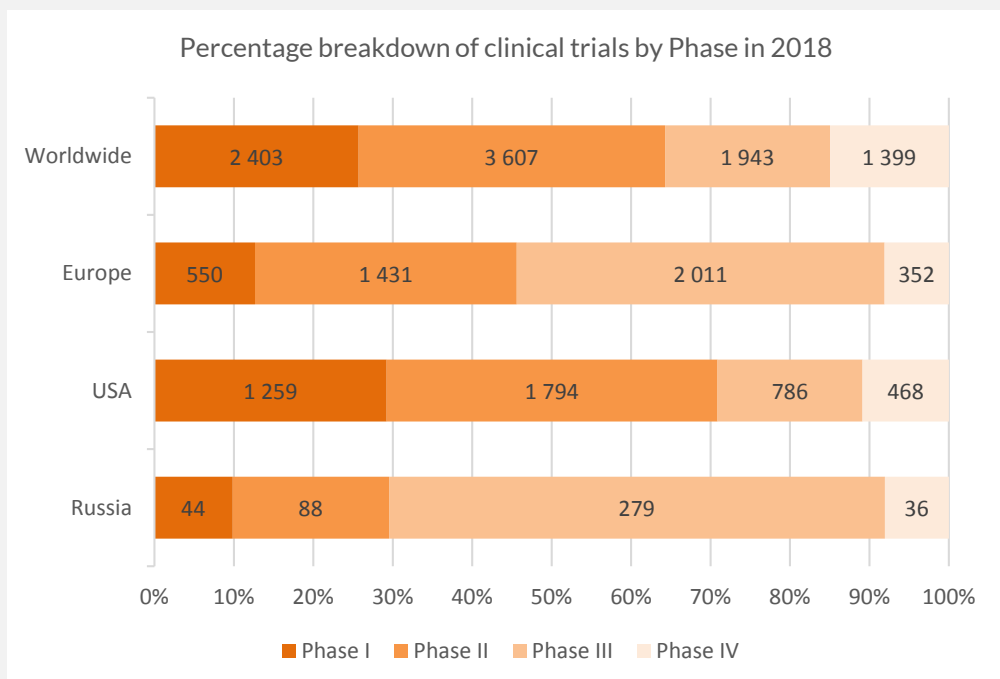
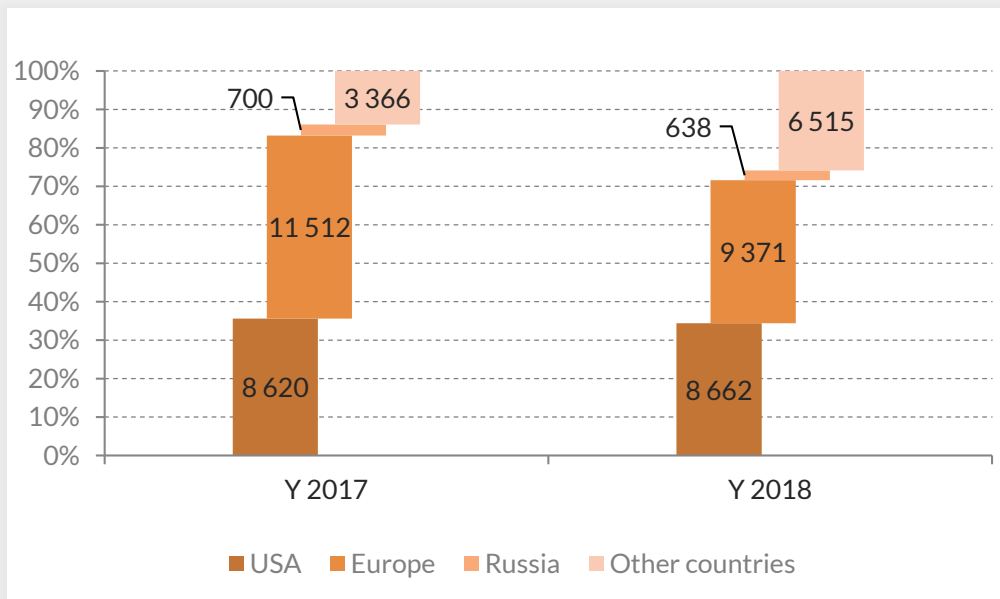


TRIAL DATA



Breakdown by region of origin

The proportions between different regions (USA, Europe, Russia, Other Countries) for trials conducted in 2018 changed in comparison to 2017. Notably, the market share of leading European countries by number of initiated studies dropped down to 37% (from 47% in the year 2017).



TRIAL DATA

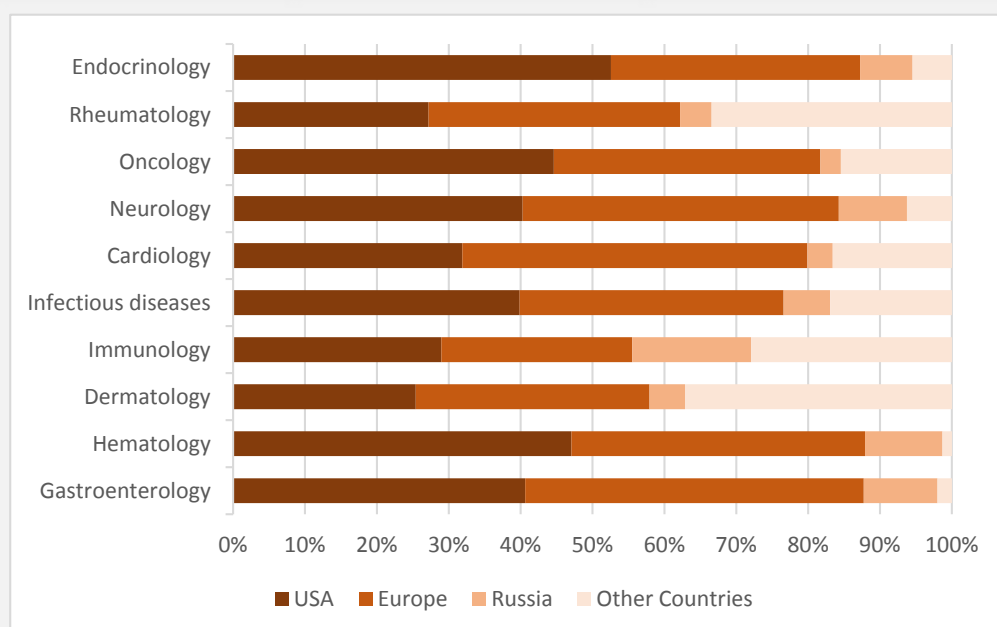
Therapeutic areas of clinical trials worldwide



In the year 2018, the largest number of studies were initiated in Oncology (4681 studies), Cardiology (1386 studies), and Infectious Diseases (803).

More than one therapeutic area could be assigned to a trial. BE studies were not included in any therapeutic area group.

Therapeutic Area	No. studies in Q4 2018	No. studies in Y 2018
Oncology	1 137	4 681
Cardiology	390	1 386
Infectious Diseases	208	803
Rheumatology	193	640
Dermatology	76	606
Neurology	201	591
Endocrinology	140	548
Gastroenterology	148	497
Hematology	91	306
Immunology	51	290
Other	4 136	14 838





WORLDWIDE CLINICAL TRIALS

Sponsor Data

The Top-10 list of global Sponsors of clinical trials worldwide remains unchanged for the past 5 years – this fact may be explained by the significant and continuously increasing amount of investment required for research and development of new drugs.

However, it's remarkable that the combined market power of these leading pharmaceutical corporations accounts for 40% of all patients enrolled in interventional clinical trials where the study Phase has been identified.

Here are the top-10 global sponsors by total number of studies initiated in Y 2018

No	Company Name	No. studies	No. patients
1	Novartis	85	24 374
2	Merck	83	30 994
3	Pfizer	76	21 186
4	Janssen	74	11 582
5	Eli Lilly	68	22 998
6	GlaxoSmithKline	68	26 876
7	Sanofi	63	29 818
8	Hoffmann-La Roche	62	19 343
9	AstraZeneca	41	30 665
10	Bayer	53	6 542
Combined market share of top-10 companies		8%	11%

Note: Observational clinical trials and clinical trials without U.S. FDA-defined Phases (from I to IV) were not included within this ranking.



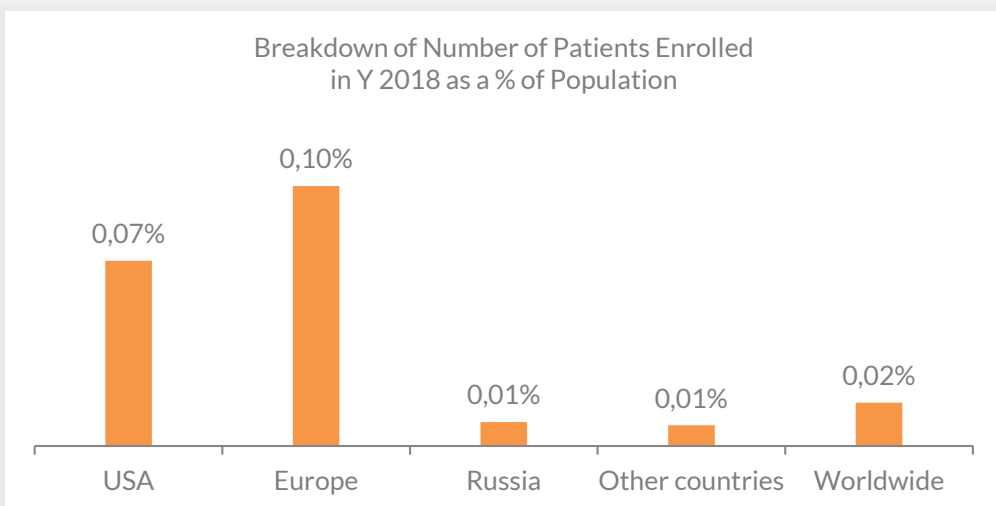
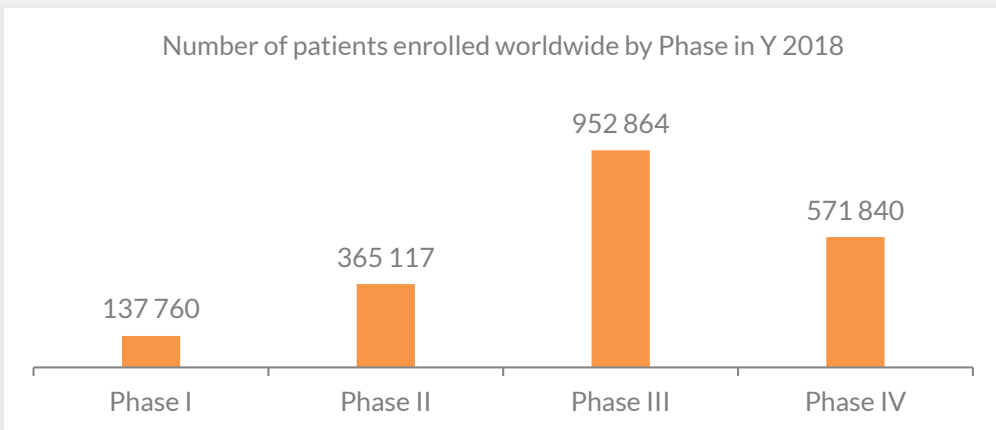


WORLDWIDE CLINICAL TRIALS

Patient Data

The total number of patients enrolled in Clinical trials of all types in the year 2018 exceeded 2 million individuals.

The majority of patients were enrolled in Phase III trials, and the largest proportion of the global patient population were Europeans. However, the share of patients participating in clinical trials remains extremely low in comparison with overall size of the population - with approximately 0,02% Worldwide.



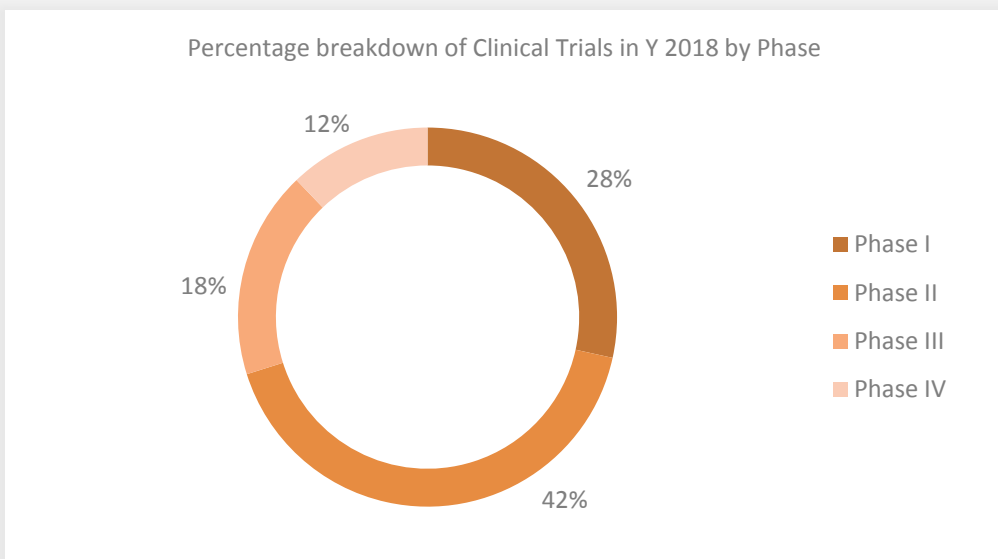
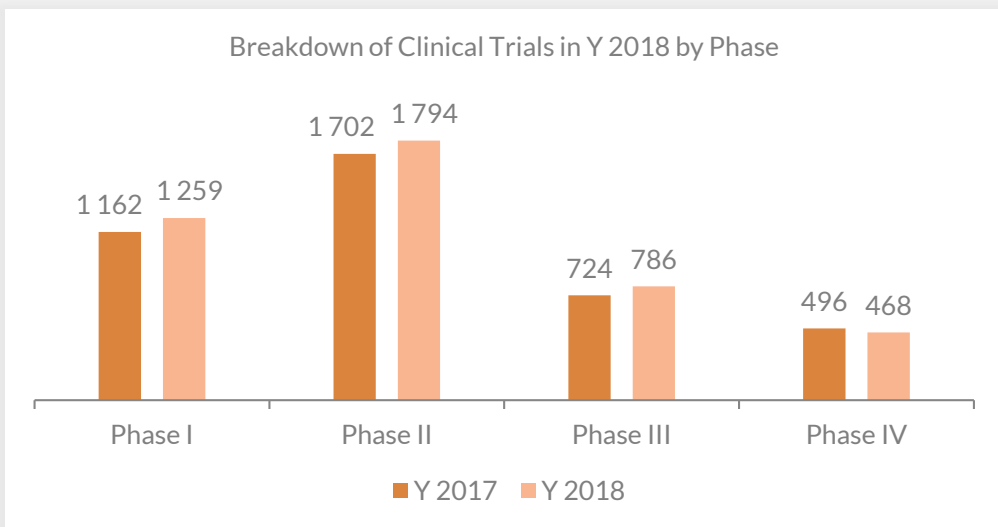


CLINICAL TRIALS IN USA

Trial Data

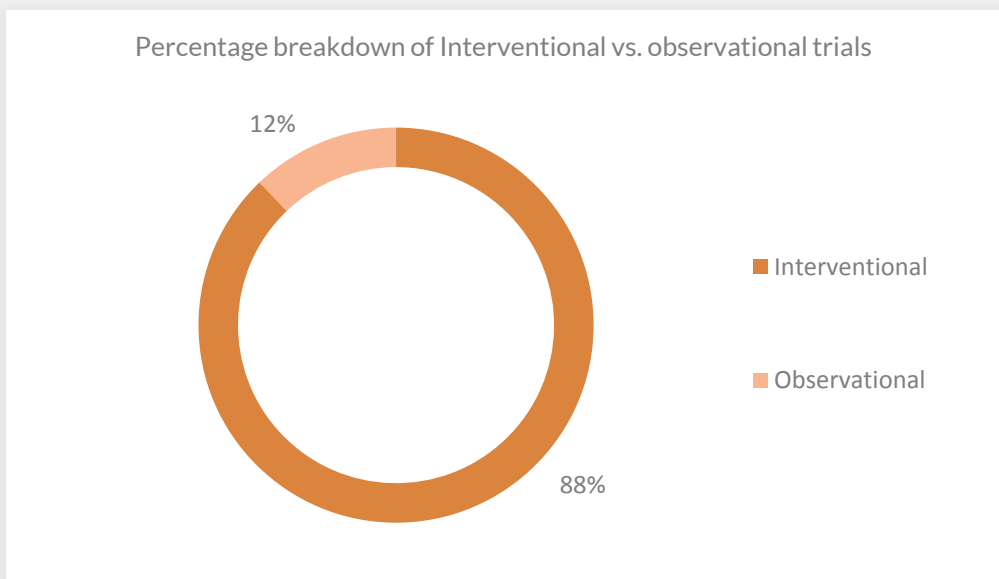
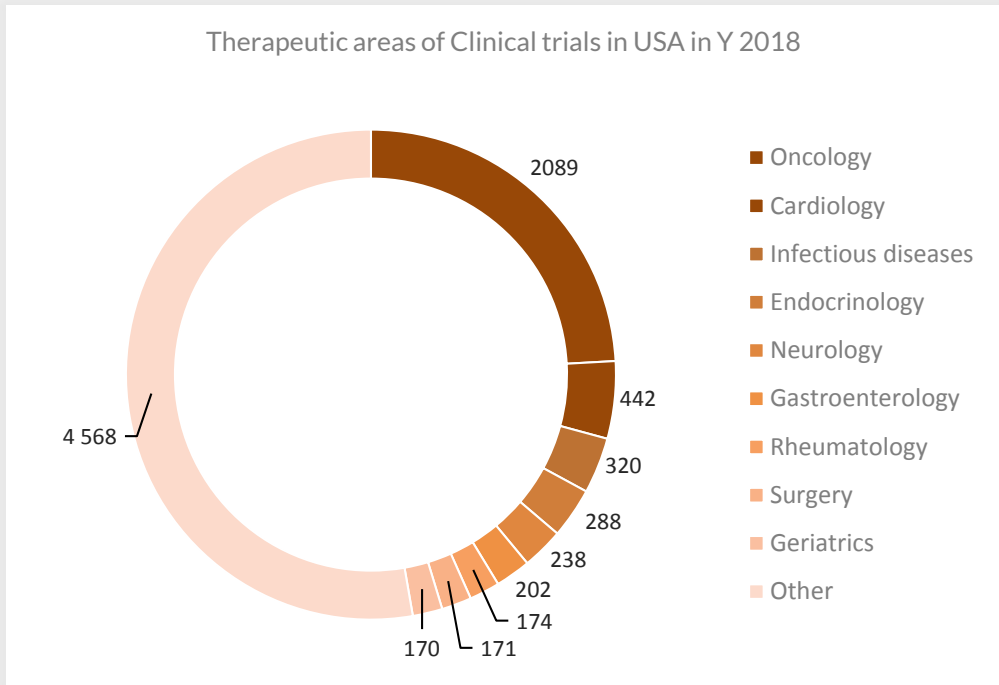
During the year 2018 there were 8,662 clinical initiated in the USA, including local and bioequivalence studies. That closely matches the previous year, when 8,620 studies were initiated. The most prevalent type of clinical trials conducted in US sites were interventional studies with a 90% market share.

The most frequent phase of clinical trials conducted across US sites by number of studies was Phase II.



The largest number of clinical trials initiated in the USA in the year 2018 were related to Oncology (2089 studies), Cardiology (442 studies), Infectious diseases (320 studies), Endocrinology (288) and Neurology (238). Other popular areas include Gastroenterology, Rheumatology, Surgery and Geriatrics.

The majority of Clinical trials conducted in the USA in Y2018 were Interventional.





CLINICAL TRIALS IN USA

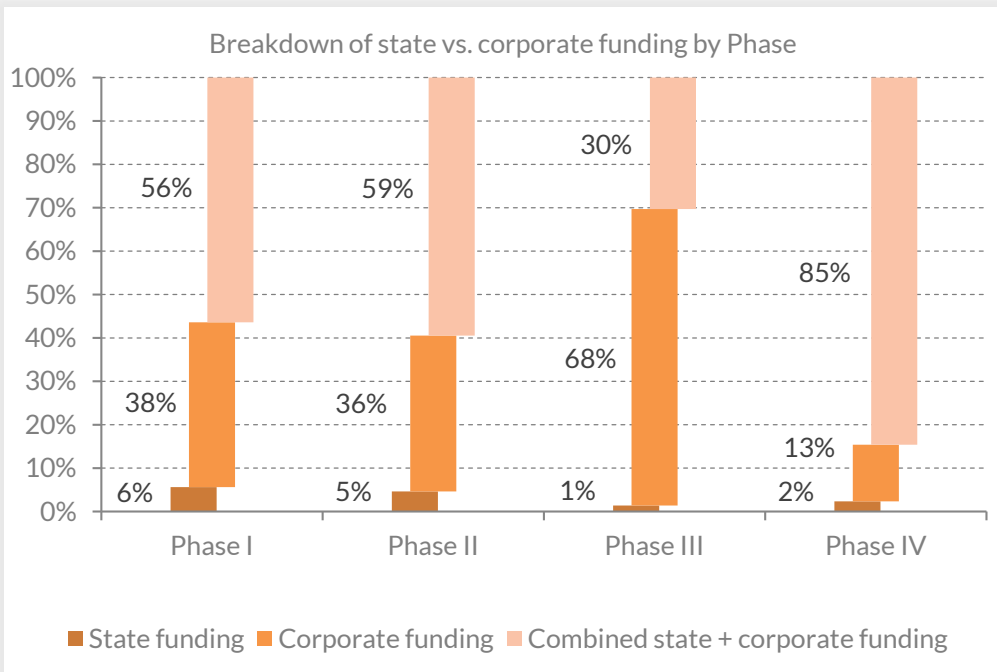
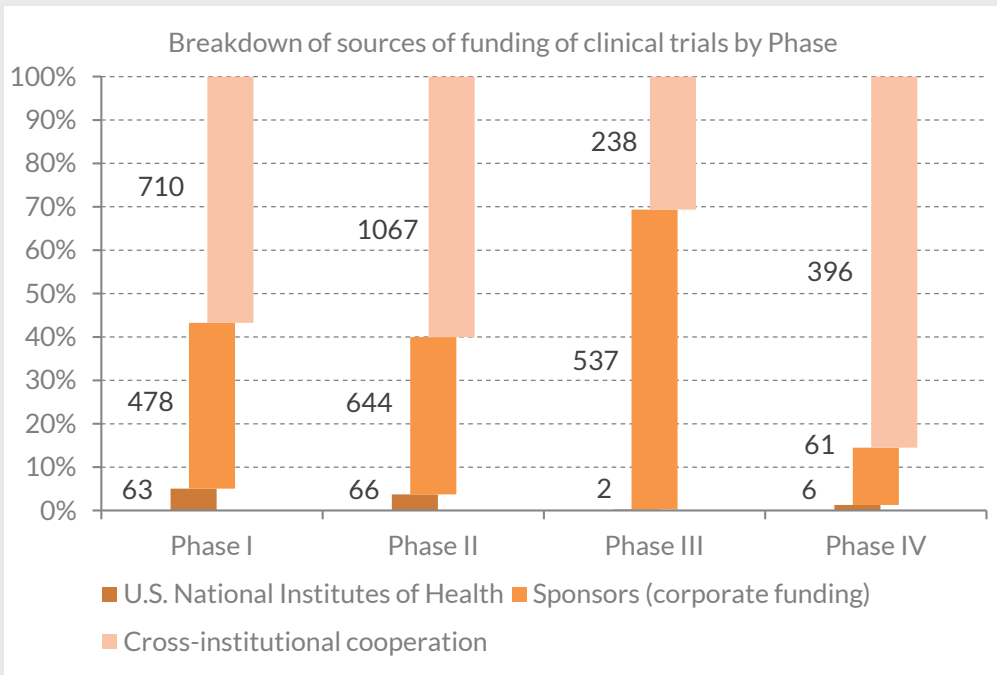
Sponsor Data

The most prevalent country of origin of pharmaceutical company sponsored clinical trials initiated in the USA in the year 2018 was the USA. The headquarters of the most active foreign companies are located primarily in Europe - in Switzerland (Hoffmann-La Roche) and the UK (AstraZeneca).

No	Company Name	No. studies	No. patients
1	Pfizer	48	18 050
2	Merck	41	22 904
3	Hoffmann-La Roche	41	14 023
4	Janssen	37	8 276
5	Eli Lilly	36	15 548
6	Bristol-Myers	34	7 061
7	AbbVie	32	9 907
8	Novartis	31	7 943
9	Bayer	23	3 661
10	AstraZeneca	22	11 256
Combined market share of top-10 companies		8%	15%



It's worth highlighting that the biggest amount of investments in clinical trials of new drugs in the U.S. is as a result of cross-institutional partnerships between the pharma business and state institutions (National Institute of Health, U.S. Federal agencies, etc.)

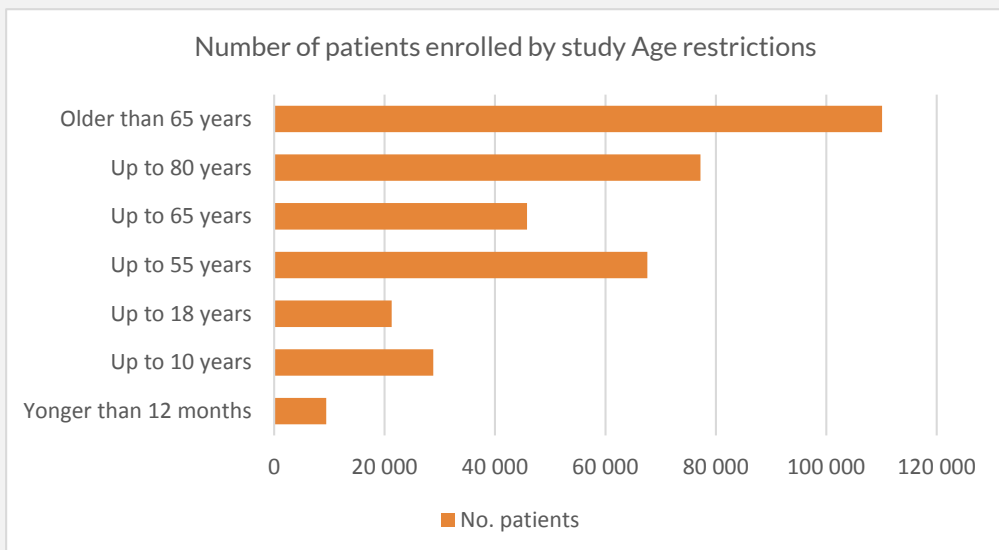
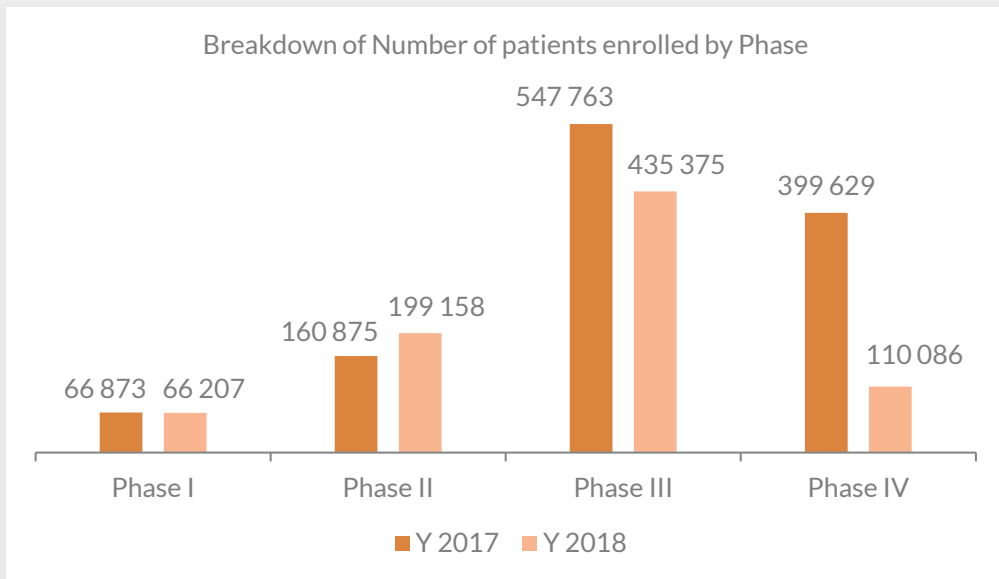




CLINICAL TRIALS IN USA

Patient Data

The overall number of patients involved in clinical trials initiated in the USA in the year 2018 reached a total of 810,826 individuals. The most prevalent phase of clinical trials by total number of participating patients was Phase II. The biggest patients' cohorts by age were "older than 65 years" and "up to 80 years".





Regulatory Data

During Q4 2018 the Center for Drug Evaluation and Research (CDER) of the U.S. FDA approved 13 new drugs as new molecular entities (NME); other approvals concerned new dosages, combinations or manufacturers

Appr.date	Drug (active ingredient)	Company
10/01/2018	Seysaranda (Sarecycline Hydrochloride)	Allergan
10/02/2018	Nuzyranda (Omadacycline Tosylate)	Paratek Pharms
10/05/2018	Tegsedinda (Inotersen Sodium)	Akcea Theraps
10/16/2018	Talzennanda (Talazoparib Tosylate)	Pfizer
10/24/2018	Xofluzanda (Baloxavir Marboxil)	Genentech
11/02/2018	Lorbrenanda (Lorlatinib)	Pfizer
11/09/2018	Yupelrinda (Revefenacin)	Mylan
11/16/2018	Aemcolonda (Rifamycin)	Cosmo Technologies
11/21/2018	Daurismonda (Glasdegib)	Pfizer
11/26/2018	Vitrakvinda (Larotrectinib)	Loxo Oncology
11/28/2018	Firdapsenda (Amifampridine Phosphate)	Catalyst Pharms
11/28/2018	Xospatanda (Gilteritinib Fumarate)	Astellas
12/14/2018	Motegritynda (Prucalopride)	Shire

Inspection Data

According to U.S. FDA data, five FDA inspections were conducted at U.S. investigative sites during Q4 2018. Four inspections ended with a No Action Indicated (NAI) outcome, and one inspection ended with a Voluntary Action Indicated (VAI) outcome.



According to the available FDA data, 300 FDA inspections were conducted at U.S. investigative sites in Y 2018 (approximately 2/3 of these inspections were conducted in the first half of the year). The majority of inspections resulted in NAI outcomes and 70 inspections resulted in VAI



About Synergy

With its unique prevolutionary mind-set, Synergy is now the World's First Agile Risk Based CRO.

Prevolution is the implementation of thoughtful premeditated change resulting from the anticipation and analysis of future trends before they happen – in other words, being 'one step ahead of evolution'.

The high recruitment rates of the emerging markets combined with innovative technology allows our clients conduct faster, cost-effective studies without sacrificing quality. We replace outdated R&D strategies by novel, more efficient approaches to clinical research.

