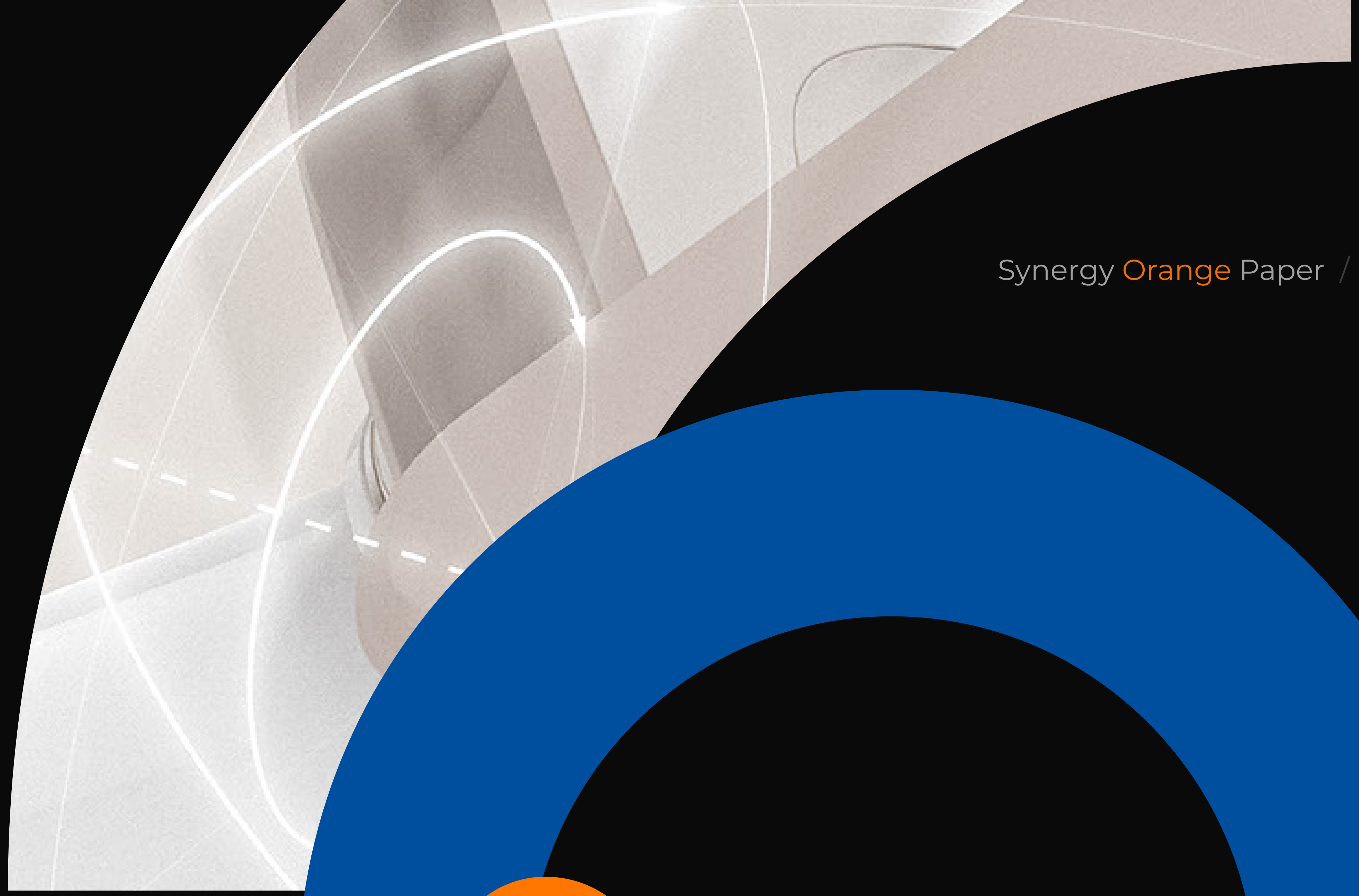
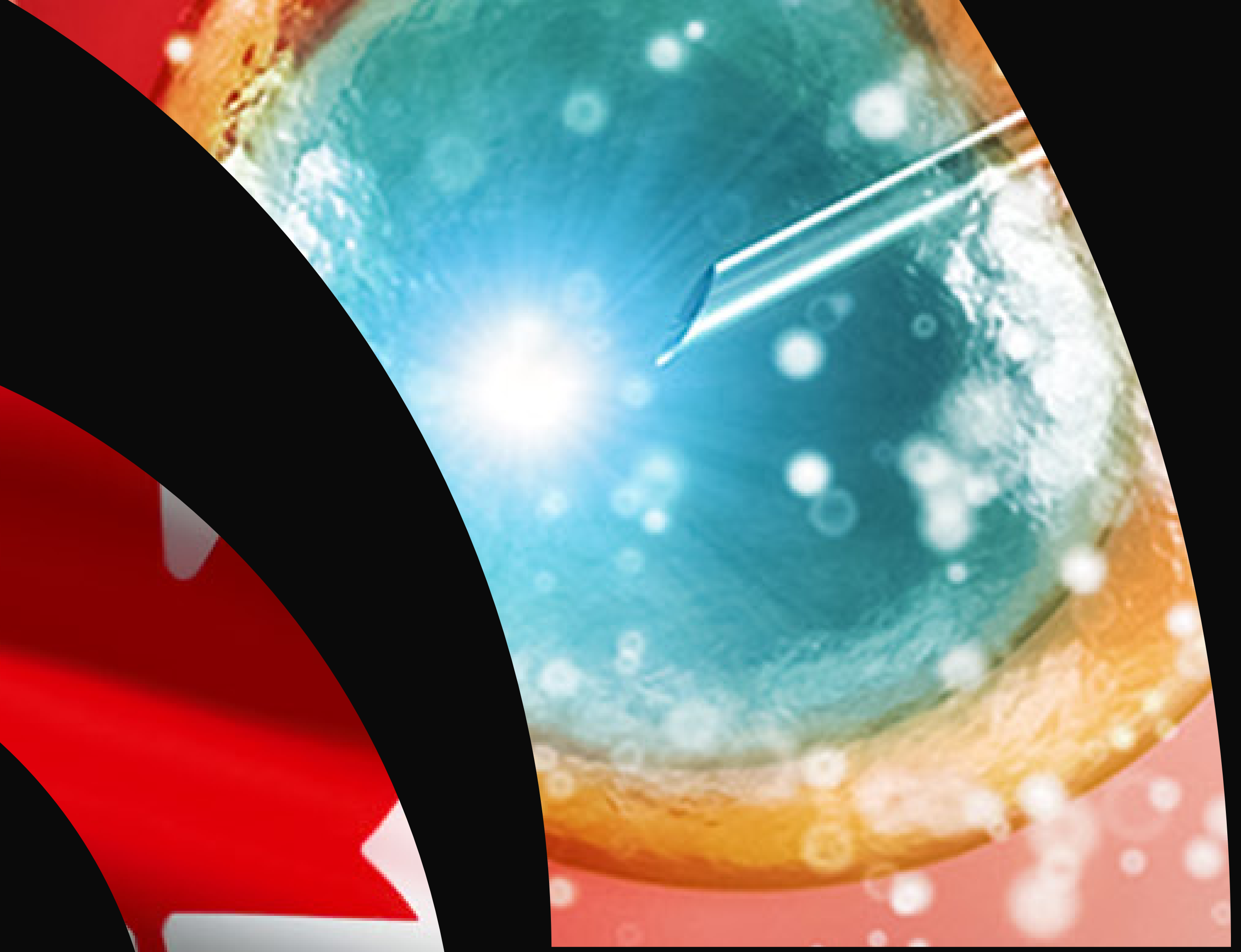
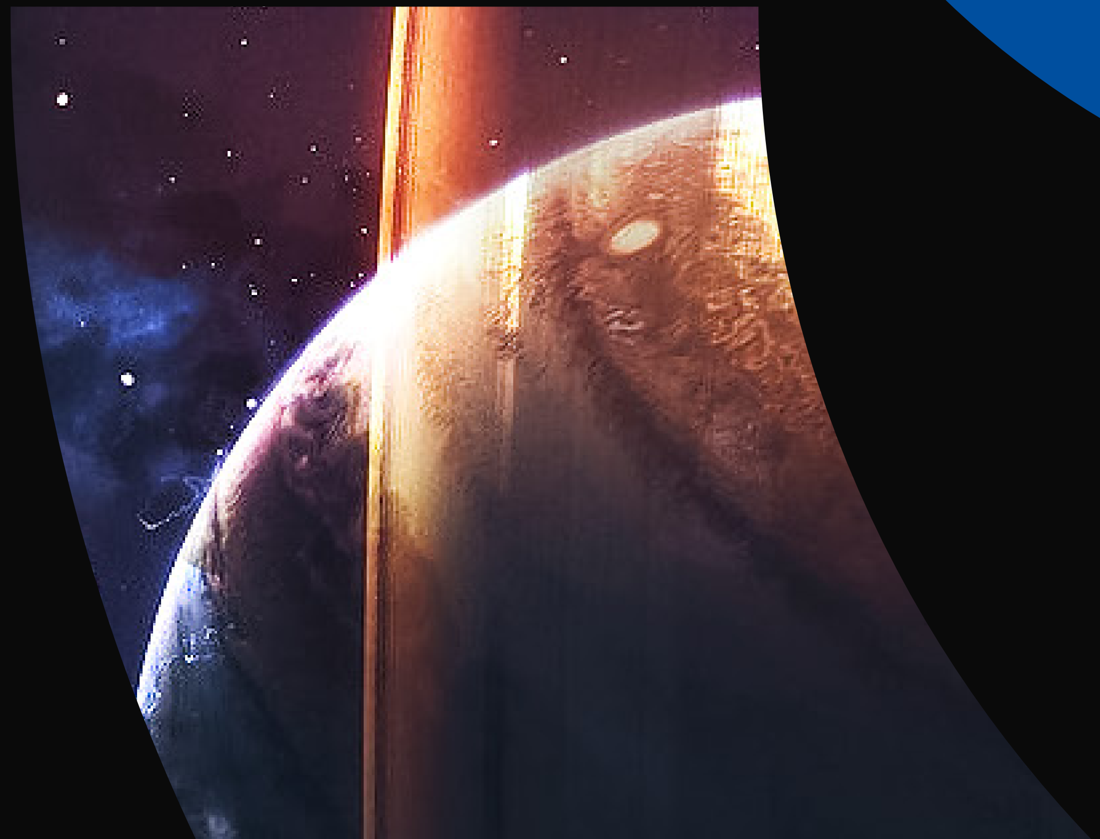




Synergy Orange Paper / 2019 autumn / quarter 3

Clinical trials in Canada

Research report



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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.

All of the data within this document are actual on date: 01/10/2019

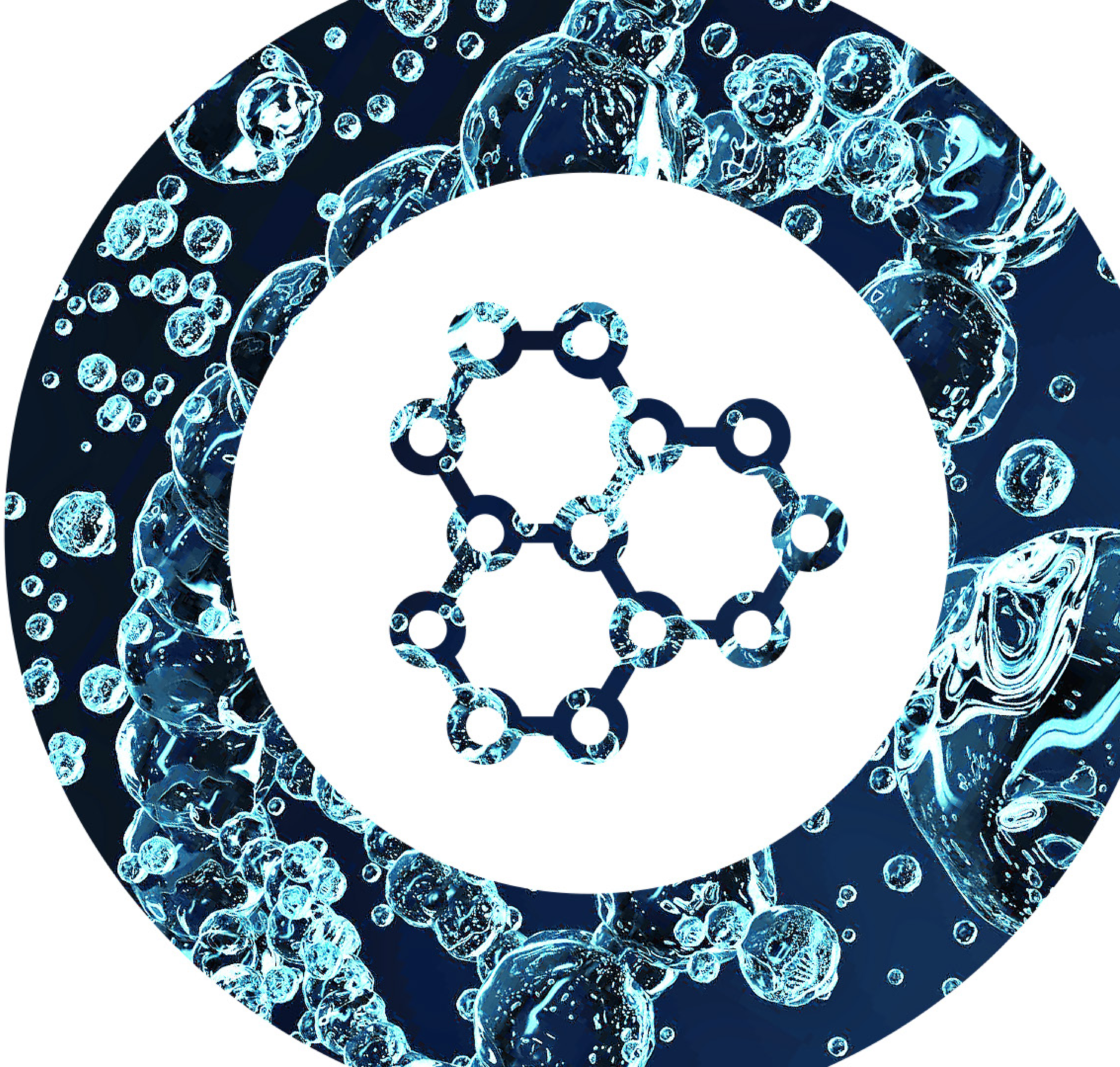


Table of Contents

Executive Summary

During Q3 2019 the official FDA website showed approvals for the initiation of 7,145 new clinical trials of all types worldwide, including local and bioequivalence studies. The number of studies initiated in Canada dropped slightly to 325 with a 16% decline rate in comparison with Q3 2018.

The dominant type of clinical trials conducted in Q3 2019 were Interventional clinical trials with 81% market share worldwide and 85% market share in Canada. The most prevalent phase of clinical trials conducted worldwide by number of studies was Phase II.

In Canada the Top-10 Sponsors combined accounted for 25% of the total number of clinical trials with an FDA-defined Phase, and for 62% of all subjects enrolled during the quarter.

In comparison, in the U.S. the top-10 Sponsors combined accounted for 15% of initiated studies and for 27% of enrolled subjects.

The total number of subjects enrolled in clinical trials worldwide of all types in Q3 2019 reached 1.02 million subjects. The most prevalent Therapeutic areas of clinical trials were Oncology, Cardiology and Mental health.

During Q3 2019 the Health Products and Food Branch of Health Canada authority approved 15 new drug applications. At the same time the authority reviewed 66 applications for marketing authorization for new medical devices, all of which were approved.

In Q3 2019 the Center for Drug Evaluation and Research (CDER) of the U.S. FDA approved 29 new drugs, including 13 new molecular entities (NME); other approvals concerned new dosages, combinations or manufacturers.

Section 1

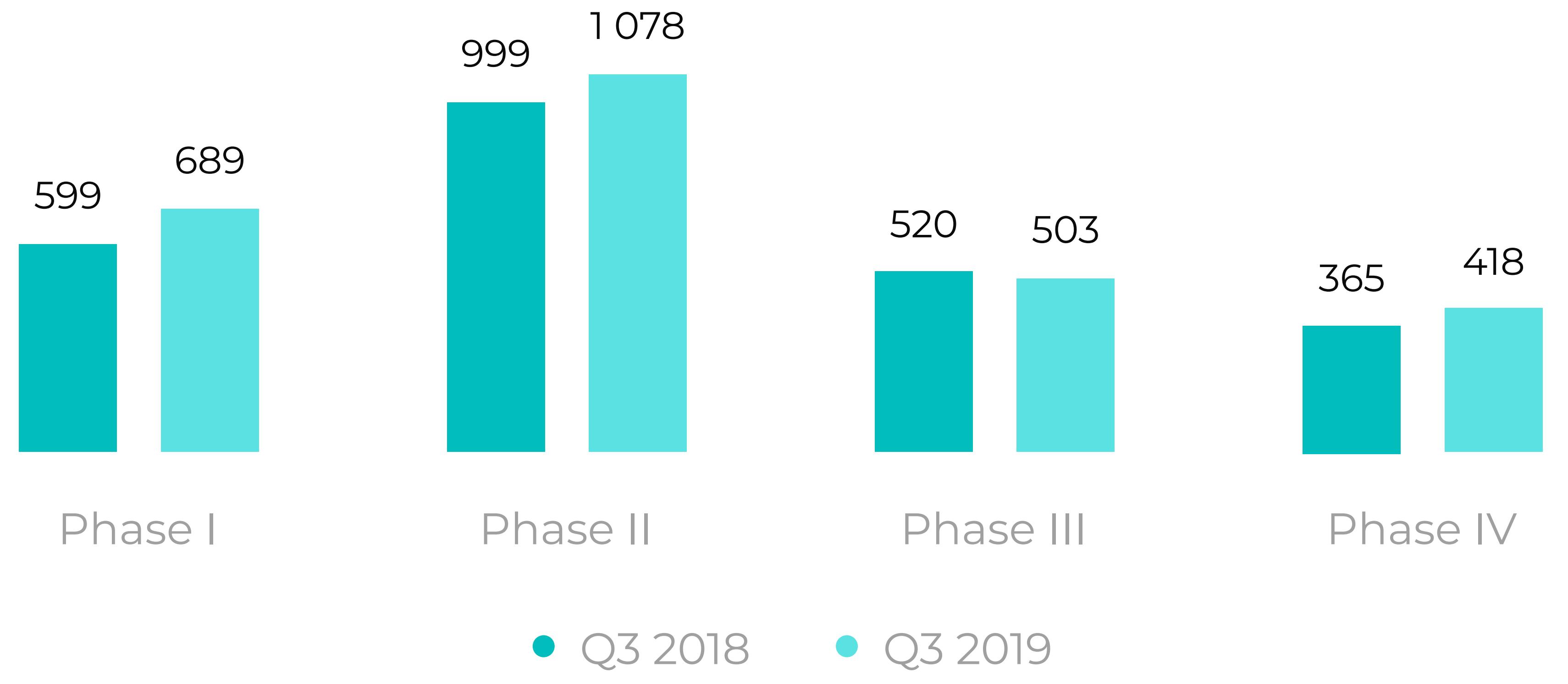
Global Clinical Trials Trial Data

During Q3 2019 the official FDA website showed approvals for initiation of 7,145 new clinical trials of all types worldwide, including local and bioequivalence studies with an overall year on year growth rate of 12% driven in large by an increasing number of trials in developing countries.

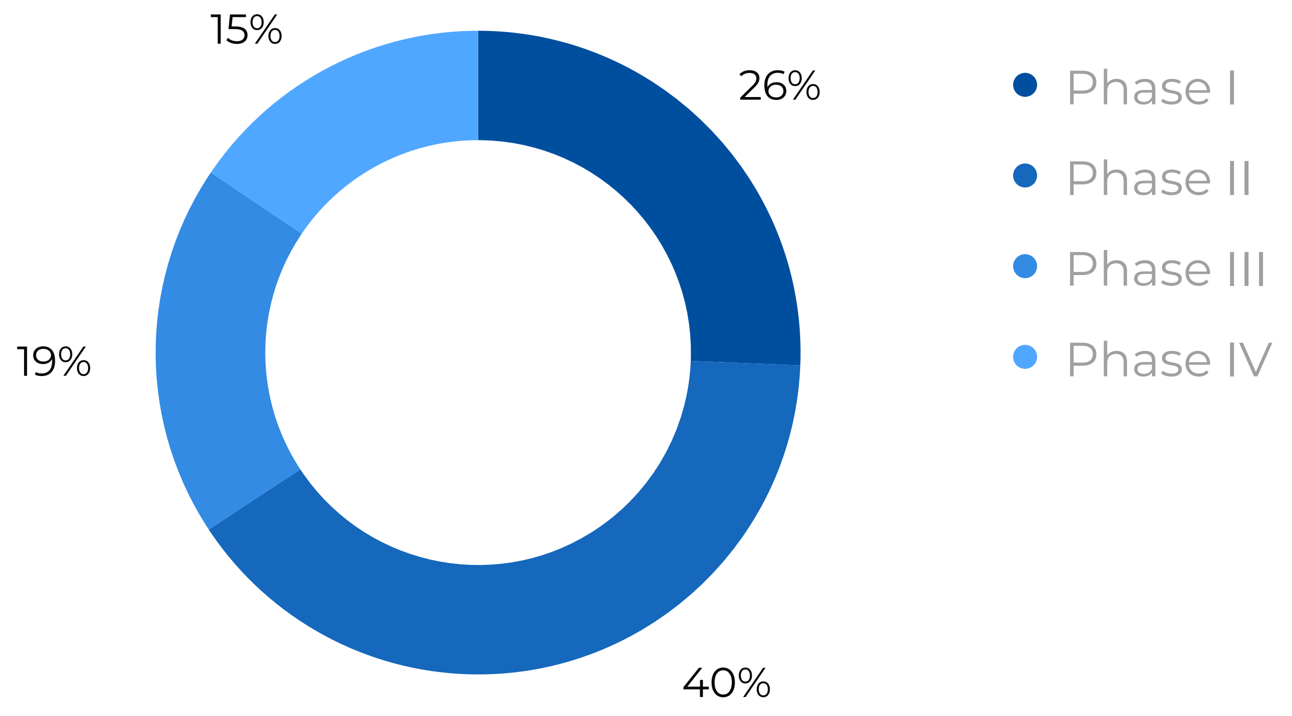
The combined market share of the U.S. and European countries by number of global initiated studies remains stable with 63% in Q3 2019, with the U.S. having 32% and Europe having 31%.

81% of all global clinical trials initiated in Q3 2019 were Interventional clinical Trials.

Breakdown of clinical trials by Phase during Q3 2019



Percentage breakdown of global clinical trials by Phase

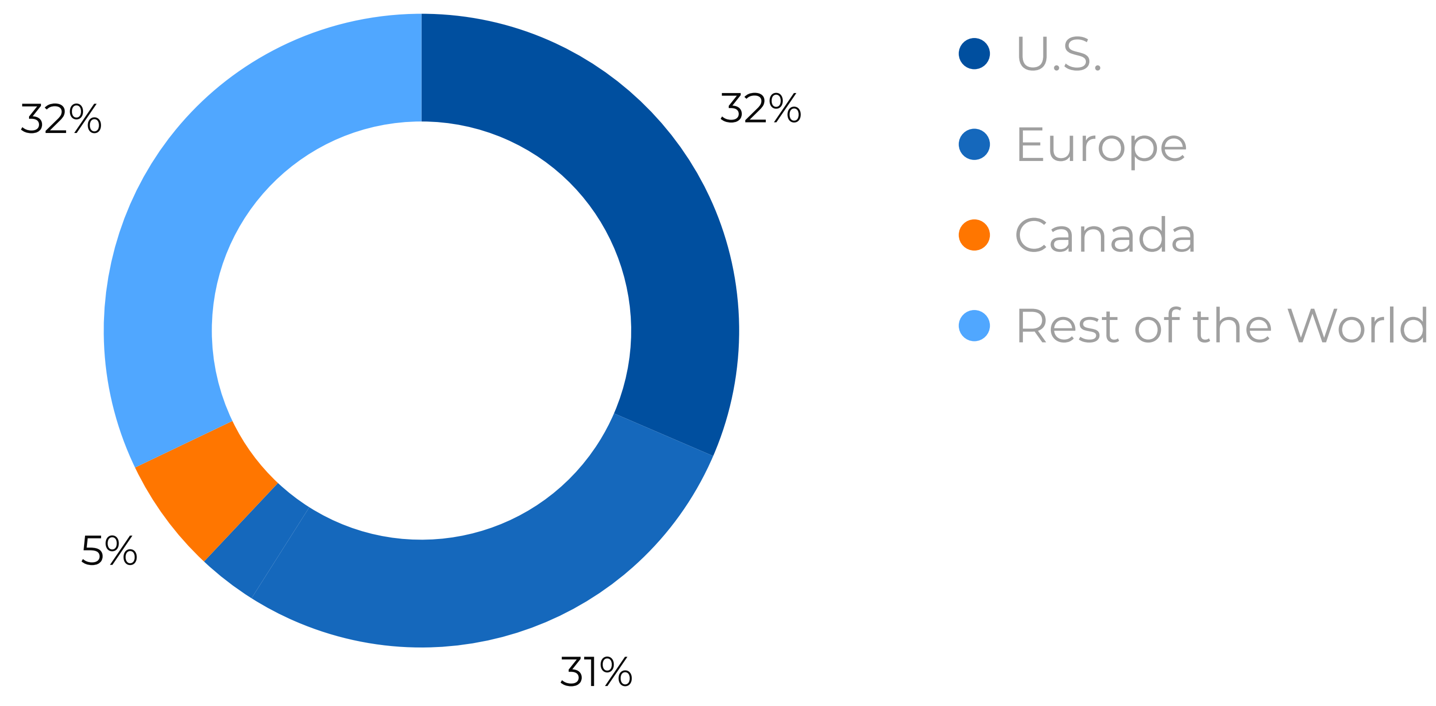


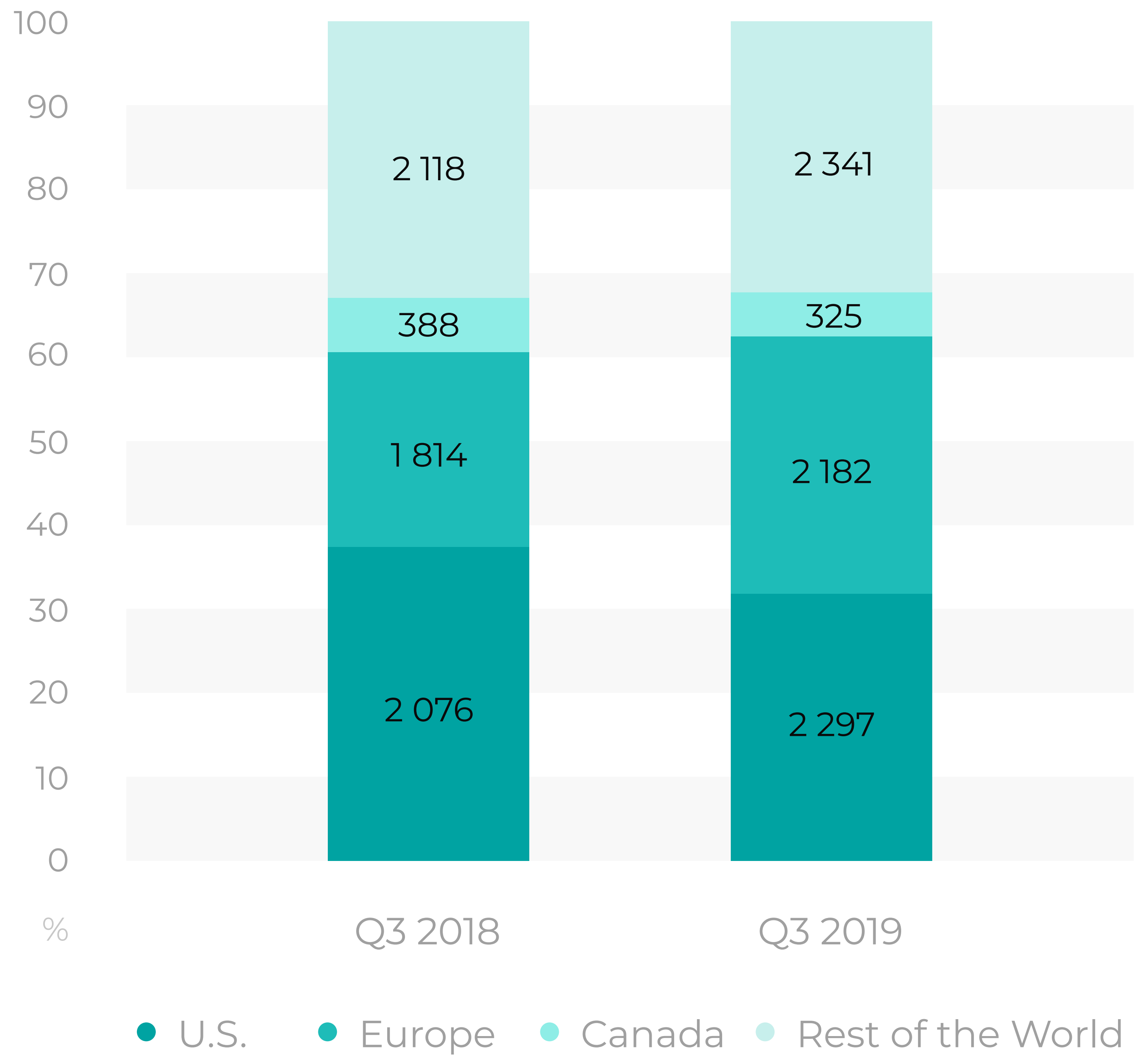
Trial Data

Breakdown by Region of Origin

The proportion of clinical trials between different global regions (i.e. U.S., Europe and Rest of the World) in Q3 2019 remains almost the same in comparison to Q3 2018.

Percentage breakdown of global clinical trials by Region





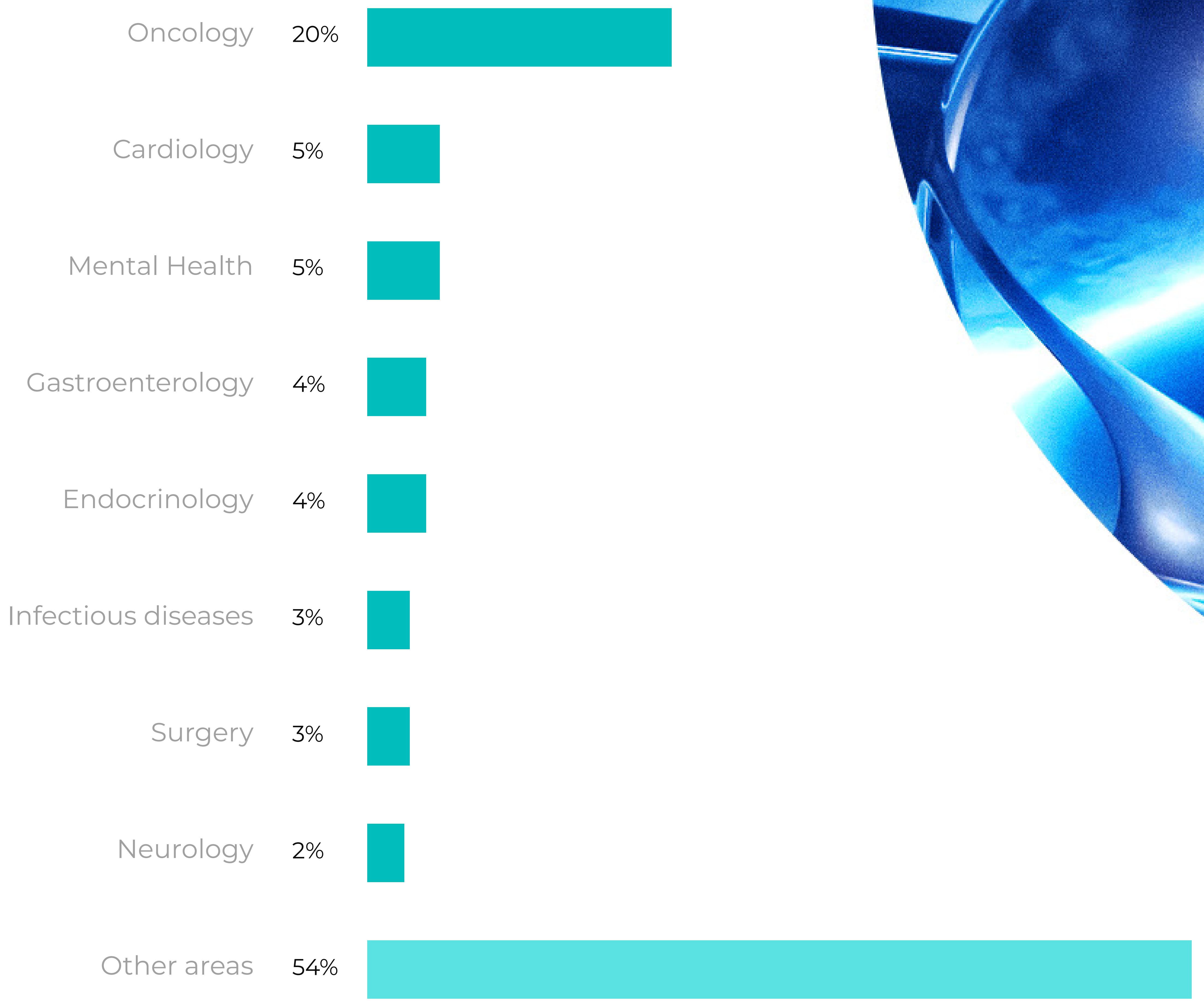
Synergy orange paper

Trial Data

Therapeutic Areas of global clinical trials

In Q3 2019 the largest number of studies were initiated in Oncology (1,149 studies), Cardiology (305 studies), Mental health (274 studies) and Gastroenterology (247 studies).

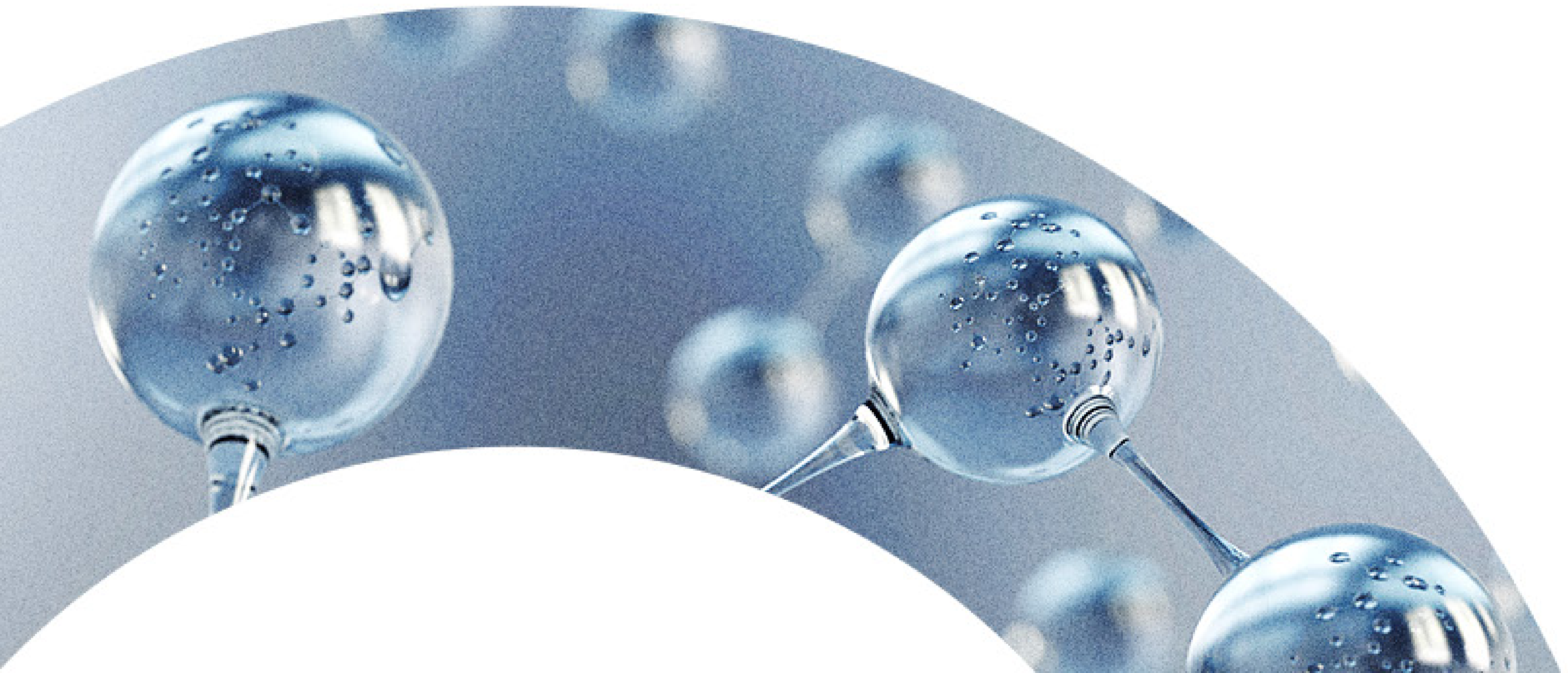
More than one therapeutic area could be assigned to a trial. BE studies were not included in any therapeutic area group.



Sponsor Data

The Top-10 list of global Sponsors of Clinical Trials worldwide has remained almost unchanged for the past 5 years – however there is now a Chinese newcomer, Jiangsu Hengrui Corporation which has appeared in this list for the first time.

However, it's remarkable that the combined market power of these leading pharmaceutical corporations accounts for just 12% of all interventional clinical trials worldwide where the study Phase has been identified, and just 8% of all enrolled subjects.



Top-10 global sponsors by Total Number of Studies Initiated in Q3 2019

№	Company Name	No. studies	No. subjects
1	AstraZeneca	50	6 561
2	Merck	43	12 844
3	Bristol-Myers Squibb	39	8 007
4	Pfizer	36	4 395
5	Janssen	36	15 124
6	Novartis	30	9 756
7	Eli Lilly	29	6 877
8	Jiangsu Hengrui	28	4 265
9	GlaxoSmithKline	22	5 914
10	Astellas Pharma	20	3 953
Combined market share of top-10 companies		**12%**	**8%**

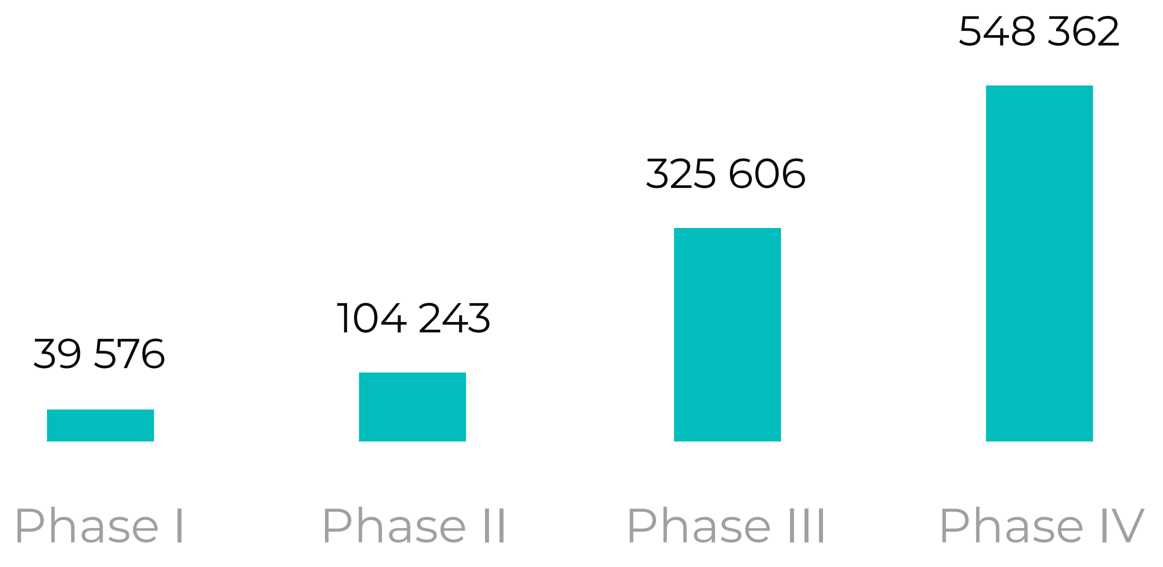
Subject Data

The total number of subjects enrolled in clinical trials of all types in Q3 2019 reached 1,017,787 subjects.

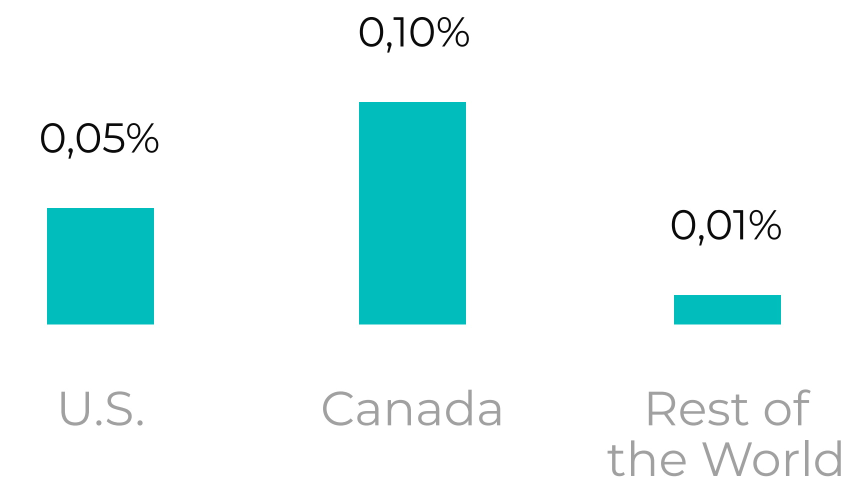
The majority of subjects were (or planned to be) enrolled in Phase IV trials, and the largest proportion of the global subject population were from the U.S.

However, the share of subjects participating in clinical trials remains extremely low in comparison with overall size of the population – with approximately 0,01% Worldwide.

Number of Subjects Enrolled Worldwide by Phase in Q3 2019



Breakdown of Number of Subjects Enrolled as a % of Population



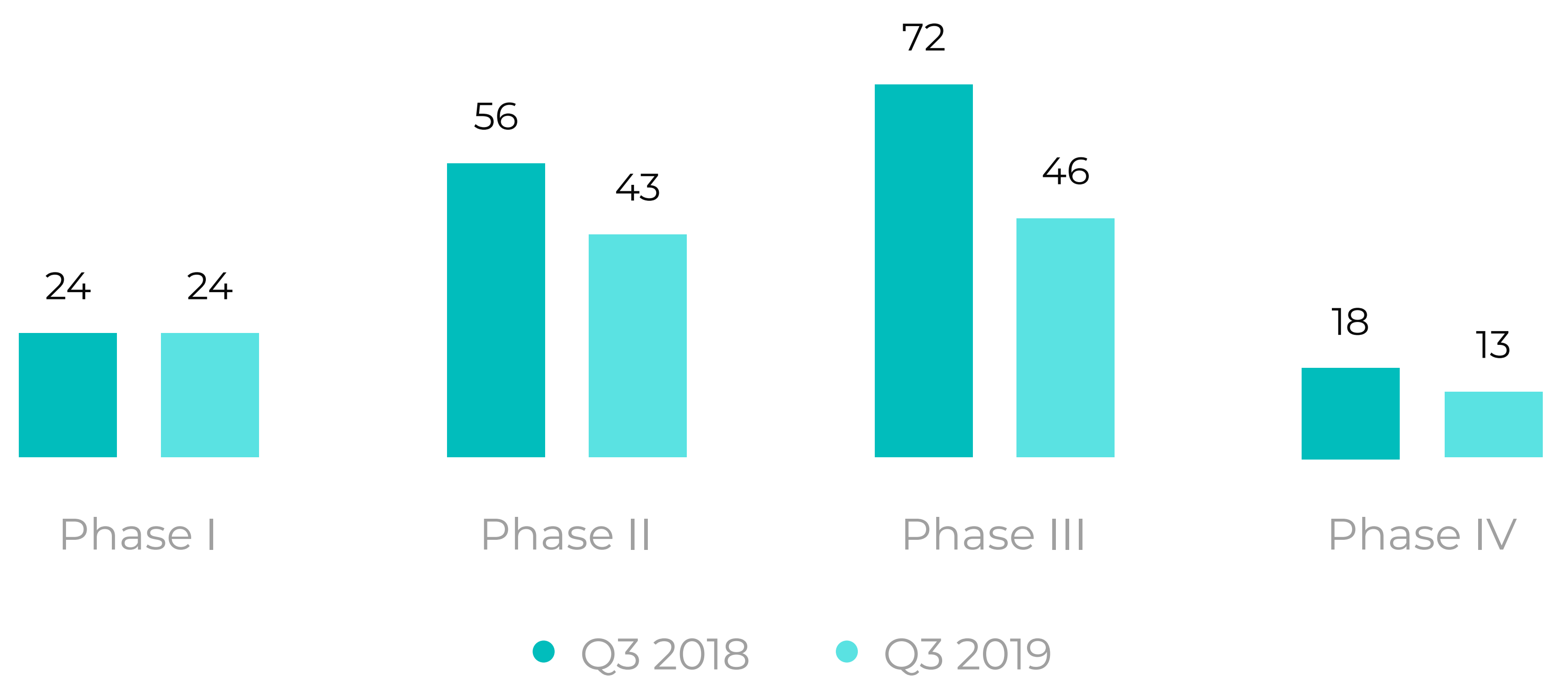
Clinical Trials in Canada Trial Data

During Q3 2019 there were 325 clinical trials initiated in Canada including local and bioequivalence studies. That represents a 16% decline in comparison with the previous year when 388 studies were initiated. If one excludes bioequivalence studies and studies without an FDA-defined Phase, there were only 170 clinical trials initiated in Q3 2018 and 126 studies initiated in Q3 2019.

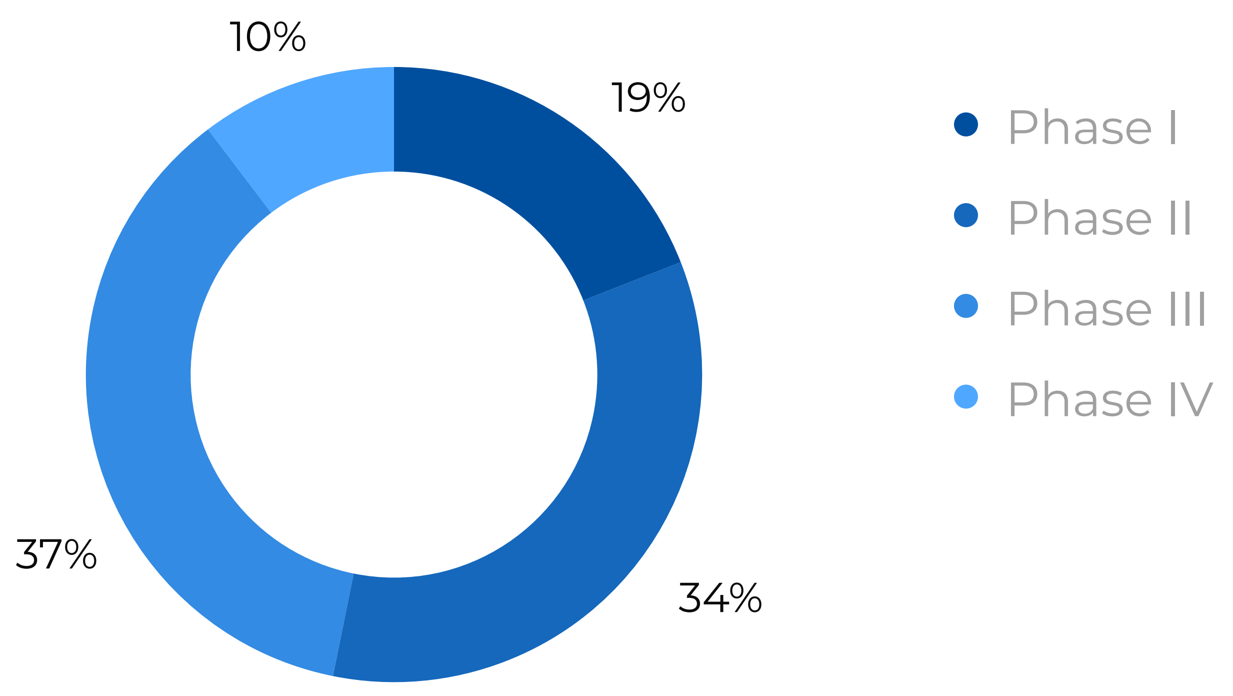
The most prevalent type of clinical trials conducted in Canadian sites were interventional studies with a 85% market share.

The most frequent phase of clinical trials conducted across the Canadian sites by number of studies was Phase III.

Breakdown of clinical trials in Canada during Q3 2019 by Phase



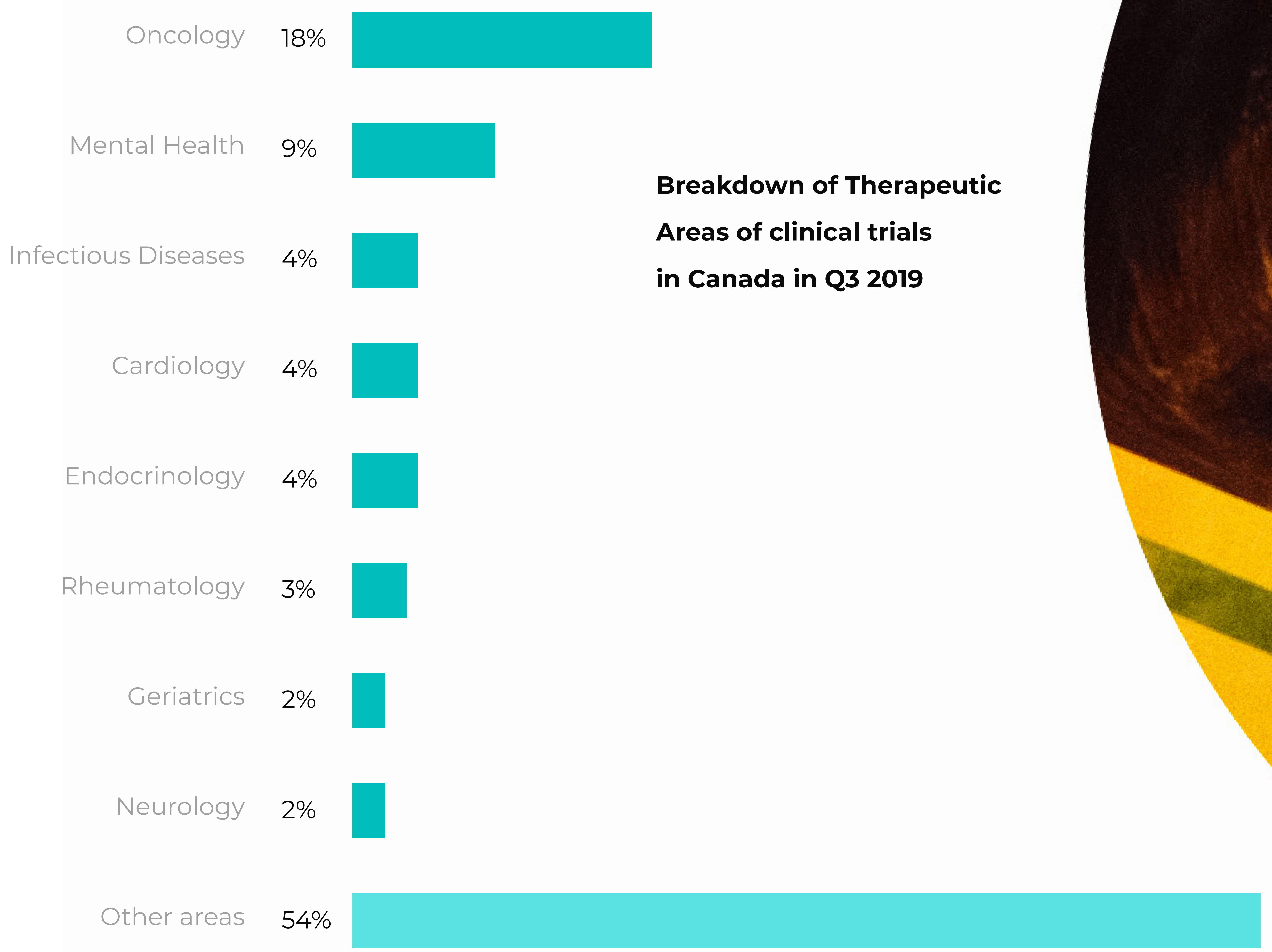
Percentage breakdown of clinical trials in Canada by Phase



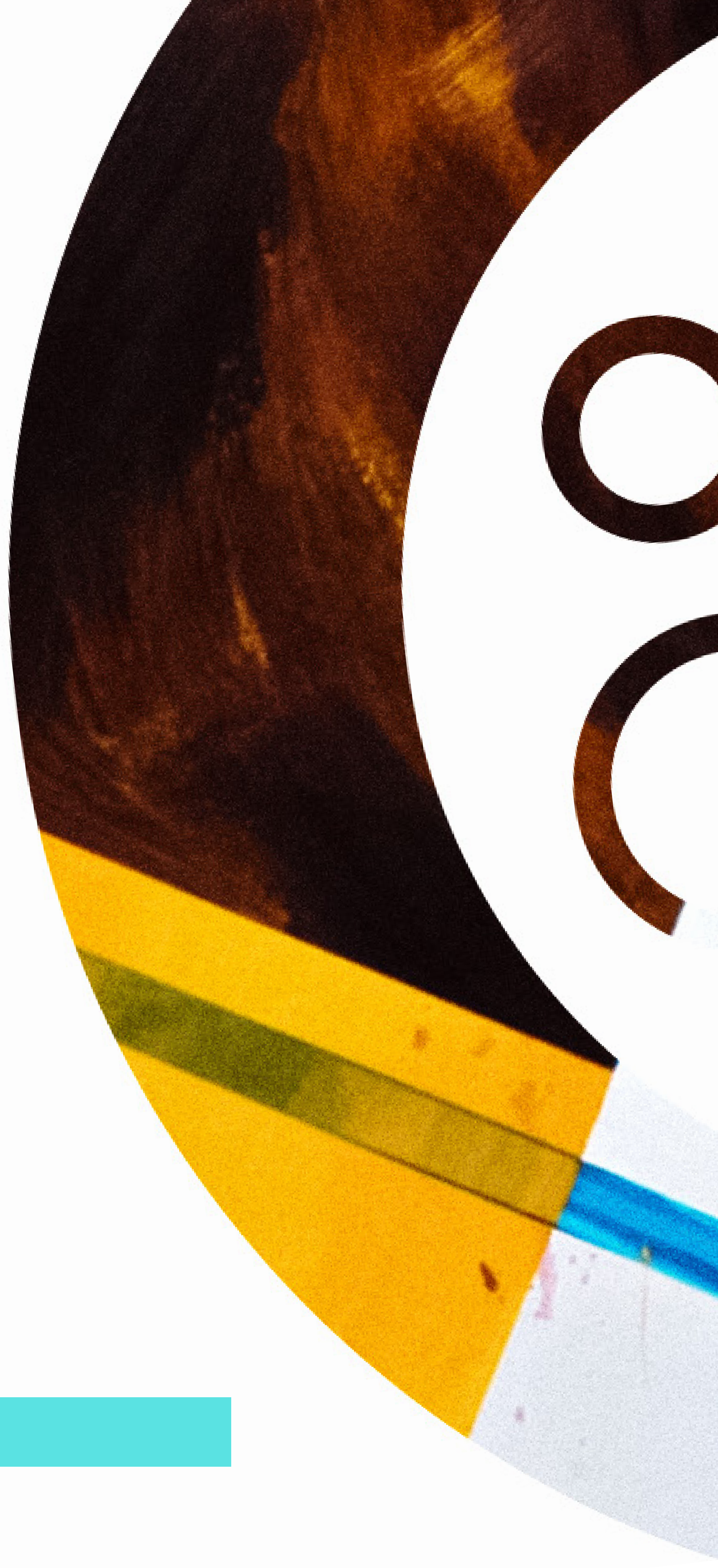
Trial Data

The largest number of clinical trials initiated in Canada in Q3 2019 were related to Oncology (50 studies), Mental health (24 studies), Infectious diseases (11 studies), Cardiology (10 studies) and Endocrinology (10 studies). Other prominent therapy areas included Rheumatology, Geriatrics and Neurology.

The majority of clinical trials conducted in Canada in Q3 2019 were Interventional.



Breakdown of Therapeutic Areas of clinical trials in Canada in Q3 2019



Sponsor Data

The most prevalent country of origin of pharmaceutical company sponsored clinical trials initiated in Canada in Q3 2019 was the U.S. The headquarters of the most active foreign companies are located primarily in Europe – in UK (AstraZeneca, GlaxoSmithKline), Ireland (Allergan) and Belgium (Janssen) – and in Japan (Astellas Pharma).

Observational clinical trials and clinical trials without FDA-defined phases (from I to IV) were not counted in this ranking. More than one Sponsor company may be involved in a single clinical trial.

Top-10 Sponsors of clinical trials in Canada in Q3 2019

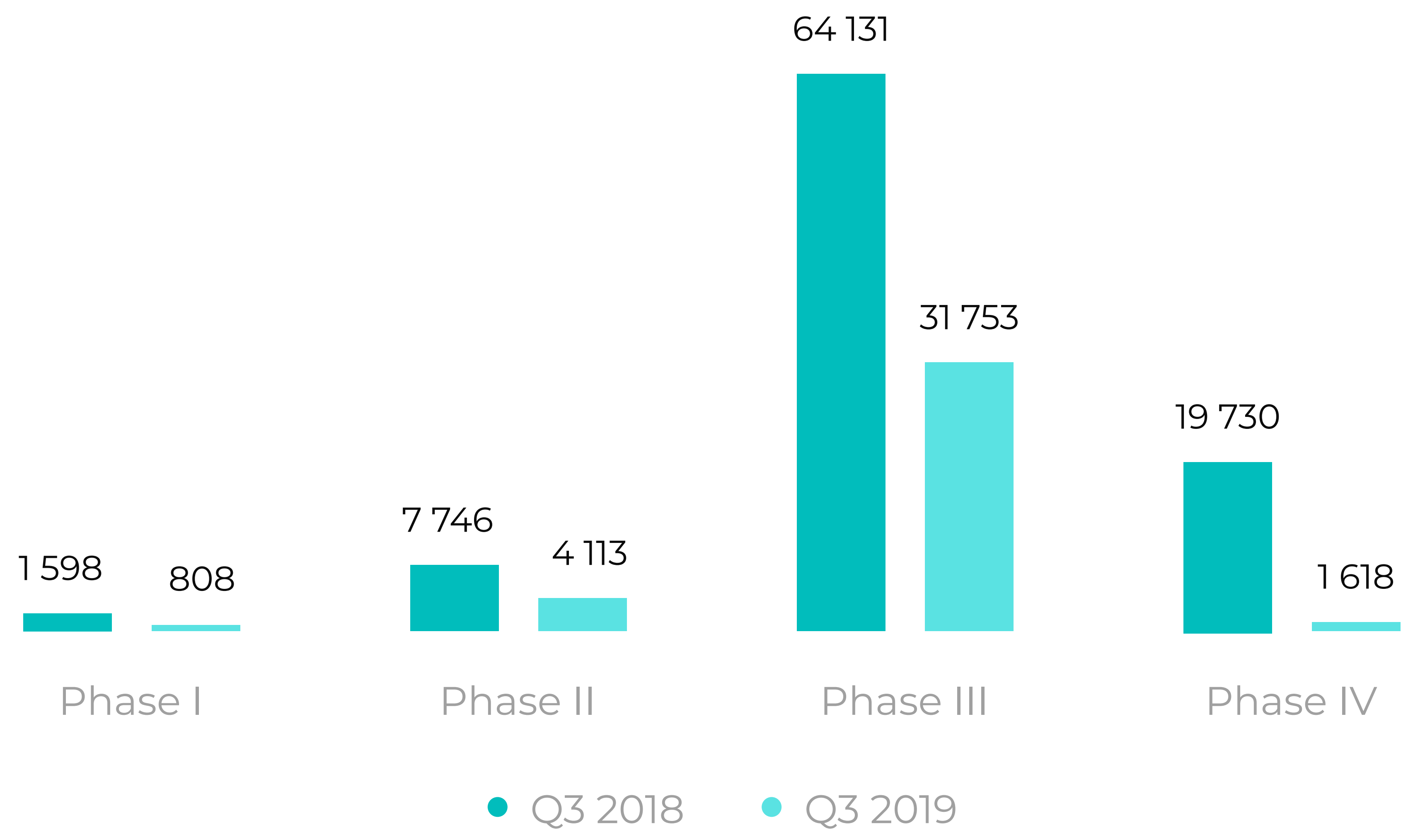
№	Company Name	No. studies	No. subjects
1	Bristol-Myers Squibb	7	5 578
2	AstraZeneca	5	2 936
3	MedImmune	3	4 612
4	GlaxoSmithKline	3	1 513
5	Pfizer	3	1 066
6	Eli Lilly	2	2 972
7	Merck	2	2 150
8	Astellas Pharma	2	1 599
9	Allergan	2	686
10	Janssen	2	516
Combined market share of these companies		**25%**	**62%**

Subject Data

The overall number of subjects enrolled (or planned to be enrolled) in clinical trials initiated in Canada in Q3 2019 (including multi-center international studies) plunged from 93,205 subjects in Q3 2018 to 38,292 subjects in Q3 2019 with year on year decline rate of 59%.

The most prevalent Phase of clinical trials by total number of participating subjects was Phase III.

Breakdown of Number of Subjects Enrolled in clinical trials in Canada by Phase



Canadian Regulatory Data

During Q3 2019 the Health Products and Food Branch of Health Canada authority approved 15 new drug applications. At the same time the authority reviewed 66 applications for marketing authorization for new medical devices, all of which were approved.

Canadian Inspection Data

According to U.S. FDA data, one FDA inspection was conducted at a Canadian investigative site during Q3 2019. The FDA representatives also reviewed the activities of the local office of Syneos Health CRO located in Montreal with no violations found (No Action Indicated - NAI result).

№	Appr. date	Drug (active ingredient)	Company
1	03/07/2019	Netspot (Gallium Dotatate)	Advanced Accelerator Applications USA
2	30/07/2019	Emgality (Galcanezumab)	Eli Lilly
3	31/07/2019	Praluent (Alirocumab)	Sanofi-Aventis
4	06/08/2019	Teriparatide (Teriparatide)	Teva
5	08/08/2019	Kevzara (Sarilumab)	Sanofi-Aventis
6	08/08/2019	Prevnar 13 (Pneumococcal 13-valent Conjugate Vaccine)	Pfizer
7	08/08/2019	Tecentriq (Atezolizumab)	Hoffmann-La Roche
8	13/08/2019	Revestive (Teduglutide)	Shire
9	15/08/2019	Trulicity (Dulaglutide)	Eli Lilly
10	16/08/2019	Actemra (Tocilizumab)	Hoffmann-La Roche
11	28/08/2019	Inflectra (Infliximab)	Celltrion
12	28/08/2019	Ultomiris (Ravulizumab)	Alexion Pharma
13	03/09/2019	Herzuma (Trastuzumab)	Celltrion
14	03/09/2019	Lemtrada (Alemtuzumab)	Sanofi-Aventis
15	20/09/2019	Keytruda (Pembrolizumab)	Merck

Health Products and Food Branch of Health Canada authority approved New Drug Applications – Q3 2019

About Synergy

Synergy Research Group is a contract research organization successfully operating in Russia, Kazakhstan, Ukraine and Canada since 2002.

The high recruitment rates of the emerging markets combined with innovative technology allows Synergy to offer our clients conduct faster, more cost-effective studies without sacrificing quality for our clients.

We have replaced outdated R&D strategies by novel, more efficient approaches to clinical research.