2019 Emerging Therapeutic Company Trend Report

Global Venture and Public Offerings, 2009-2018
Global Licensing and Acquisitions, 2009-2018
2019 Global Clinical Pipeline

by David Thomas, CFA and Chad Wessel
BIO INDUSTRY ANALYSIS

About BIO

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial, and environmental biotechnology products. BIO also produces the BIO International Convention, the world's largest gathering of the biotechnology industry, along with industry-leading investor and partnering meetings held around the world.

Access BIO Industry Analysis reports here: www.bio.org/iareports

Letter from the Honorable Jim Greenwood & Dr. Cartier Esham

With more than 90% of the biopharmaceutical industry made up of small, emerging companies, it is important for BIO to better understand early-stage investor and deal-making trends in order to determine where scientific or policy issues may be impacting the industry's ability to maintain a robust pipeline of innovative medicines. The ability to access capital and form strategic alliances is vital for small therapeutic-focused companies to succeed in translating novel drug candidates into approved medical products for patients.

In this report, we set out to highlight five investment and deal-making activities involving emerging therapeutic companies: venture capital, initial public offerings (IPOs), follow-on public offerings (FOPOs), licensing, and acquisitions. These categories are broken down by phase of development and by disease area, allowing us to gauge interest levels across a wide range of company types and financing methods. In addition, we examined the current clinical pipeline, including an analysis of partnered vs. unpartnered small company clinical programs for each major disease area.

Some of the key findings from this report are:

- **Venture Capital Investment:** A record $12.3 billion in venture funding went to U.S. emerging therapeutic companies in 2018, with 95% toward novel R&D and only 5% into drug improvement R&D for existing drugs. Venture investment into innovative U.S. therapeutic companies continues to outpace Europe (5.7x), Asia (4.6x), and the rest of the world (35x) despite a record $5.2 billion for Ex-U.S. companies. First-time Series A financing broke a record in the U.S. with 109 new companies receiving funding, indicating a robust interest in early-stage biotech.

- **IPOs:** U.S.-based R&D-stage emerging therapeutic companies were able to raise $5.1 billion from 47 IPOs in 2018, a record dollar amount and the 2nd highest number of IPOs in a decade. Ex-U.S. based R&D-stage emerging therapeutic companies raised $2.3 billion from 22 IPOs, a record dollar amount.

- **Follow-On Public Offerings:** Public market follow-on offerings for U.S.-based R&D-stage emerging therapeutic companies remained strong, with $11.5 billion raised in 2018 across 118 offerings (valued at $10 million or more). Ex-U.S.-based R&D-stage emerging therapeutic companies raised $3.2 billion from 28 transactions in 2018, a record year in dollars raised and the number of financings.

- **Licensing:** Global R&D-stage licensing deals (valued at $10 million or more) brought in $9.1 billion in upfront payments, a 107% increase over 2017. Asian emerging company assets accounted for a record 18 of these deals in 2018, albeit reaching only 11% of the total funds raised.

- **Acquisitions:** The number of global R&D-stage emerging therapeutic company acquisitions rebounded from a decade low of 21 in 2017 to 28 in 2018. A record $32.5 billion was paid upfront for the 28 R&D-stage companies. U.S.-based companies accounted for 66% of the R&D-stage emerging company acquisition targets. The number of global market-stage emerging therapeutic company acquisitions reached a decade low of four acquisitions for $2.2 billion (upfront).

- **Global Clinical Pipeline:** Total active clinical-stage programs reached a record 6,984 with emerging companies accounting for 73% of these programs. Emerging companies have 94 marketing applications for new drugs (NDA/BLAs) under review at the U.S. FDA. U.S.-based emerging companies account for 62% of these submissions.

This report will help inform our future policy work and provide industry, policymakers, and other stakeholders with a comprehensive view of the investment and partnering environment for novel therapeutics.

Sincerely,

Jim Greenwood

President & CEO, BIO

E. Cartier Esham, Ph.D.

EVP, Emerging Companies Section, BIO

EXECUTIVE SUMMARY OF 2018 DATA

Venture Capital R&D & Market-stage		$B Raised	Series A	$B Raised	A-1 #
	U.S.	$12.3	U.S.	$5.0	109
	Ex-U.S.	$5.2	Ex-U.S.	$1.5	48
	Global	$17.5	Global	$6.5	157

IPOs R&D & Market-stage		$B Raised	R&D-stage	$B Raised	#
	U.S.	$5.2	U.S.	$5.1	47
	Ex-U.S.	$2.9	Ex-U.S.	$2.3	22
	Global	$8.1	Global	$7.4	69

Follow-Ons R&D & Market-stage		$B Raised	R&D-stage	$B Raised	#
	U.S.	$17.5	U.S.	$11.5	118
	Ex-U.S.	$5.7	Ex-U.S.	$3.2	28
	Global	$23.2	Global	$14.7	146

Out-Licensing R&D-stage		$B Potential*	R&D-stage	$B Upfront	#
	U.S.	$57.7	U.S.	$7.0	98
	Ex-U.S.	$33.6	Ex-U.S.	$2.1	62
	Global	$91.3	Global	$9.1	160

Acquisitions R&D & Market-stage		$B Potential*	R&D-stage	$B Upfront	#
	U.S.	$34.7	U.S.	$24.7	18
	Ex-U.S.	$10.4	Ex-U.S.	$6.2	10
	Global	$45.1	Global	$32.5	28

Clinical Pipeline Large & ETC		April 2019	ETC Pipeline	April 2019	%
	U.S.	3,855	U.S.	3,093	44%
	Ex-U.S.	3,129	Ex-U.S.	1,974	28%
	Global	6,984	Global	5,067	73%

2018 Executive Summary of top-line data for global investment, deal-making, and clinical pipeline.

***Total potential amount for licensing and acquisitions includes contingent payments (CVRs). Emerging companies are R&D-stage and Market-stage companies with less than $1 billion in annual sales. Licensing covers only R&D-stage assets out-licensed by either R&D-stage or market-stage emerging companies. ETC= Emerging Therapeutic Company.**

Table of Contents

Introduction

In this report, we set out to identify trends affecting emerging therapeutic companies across five core areas of investment and deal-making: venture capital, initial public offerings (IPOs), follow-on public offerings (FOPOs), licensing, and acquisitions. In addition, the clinical pipeline is analyzed for each disease area, phase, and degree of industry partnering. This broad-based analysis will help identify where scientific or policy issues may be impacting the ability to maintain a robust pipeline of innovative medicines – a goal that is shared by patients, healthcare providers, policymakers, investors, and the biopharmaceutical industry alike.

We define emerging companies as those which are either in R&D-stage drug development or at market-stage but with less than $1 billion in sales. More than 95% of emerging therapeutic companies are R&D-stage without an FDA approved therapeutic product, thus the market-stage companies are a small subset. Transactions in this report are detailed by development stage and disease area of the lead product under development by the emerging company.

We analyzed the most recent 10 years of investment and deal activity (2009-2018) through rigorous annotation of data from six databases to create the broadest, most comprehensive study possible. For venture capital, the primary data source used was the Cortellis Competitive Intelligence database from Clarivate Analytics & Thomson Reuters. This was supplemented with three others: EvaluatePharma, Informa's Strategic Transactions, and BioCentury's BCIQ database. For IPOs, we populate our own database using various news sources such as Endpoints, FierceBiotech, Bioworld and Biocentury. BioCentury's BCIQ was the primary data set used for follow-on public offering data. Licensing and acquisition vetting is primarily based on Informa's Strategic Transactions, supplemented by reviewing the Cortellis Deals database from Clarivate. For the clinical pipeline we analyzed data from Informa's Biomedtracker. For further details, see the Methodology section at the end of this report.

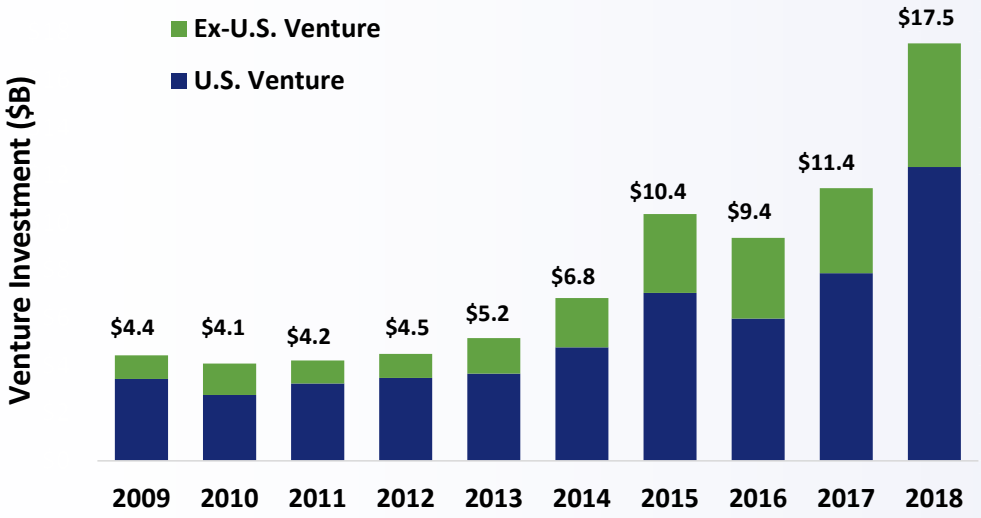
Private emerging companies working on innovative therapeutics are highly dependent on access to capital. For early-stage private companies, the majority of this investment comes in the form of venture capital until the eventual listing on a public exchange. This initial public offering is the first of what can be many rounds of financing from public investors through follow-on public offerings, financings that can provide timely access to capital after key clinical or regulatory milestones.

Licensing is also a significant source of funding for emerging companies, and often entails sharing development expertise and technical resources with a larger company. The inclusion of company acquisitions in this study aims to shed light on the degree of interest larger multinational drug manufacturers have in expanding and complementing their own pipelines through external innovation.

Venture Capital Funding

Over the last decade, a total of $78 billion in venture investment dollars went to emerging therapeutic companies globally, with a record $17.5 billion in 2018. This represents a significant increase of 54% above 2017 and is 161% above the average levels seen over the prior nine years.

VENTURE FUNDING OF EMERGING THERAPEUTIC COMPANIES WORLDWIDE, 2009-2018



VC Raised ($B)	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
USA	$3.4	$2.8	$3.2	$3.5	$3.7	$4.8	$7.1	$6.0	$7.9	$12.3
Europe	$0.8	$1.1	$0.7	$0.7	$1.2	$1.5	$2.4	$2.0	$1.8	$2.2
Asia	$0.1	$0.1	$0.2	$0.2	$0.2	$0.3	$0.5	$0.9	$1.3	$2.7
ROW	$0.1	$0.1	$0.1	$0.1	$0.1	$0.3	$0.4	$0.5	$0.5	$0.4
Global	$4.4	$4.1	$4.2	$4.5	$5.2	$6.8	$10.4	$9.4	$11.4	$17.5

Figure 1. Investment into global emerging therapeutic companies, 2009-2018, by region. Countries in Ex-US regions can be found in the Methodology section of the report.

Figure 1 shows venture capital raised in both the U.S. and Ex-U.S. In 2018, the percentage increase in venture funding of Asia-based companies was 108% above 2017 and is 575% above the prior nine-year average. European companies attracted less capital in 2018 than the peak year in 2015 ($2.2 billion vs. $2.4 billion).

Venture Capital Funding for U.S. Therapeutic Companies

As shown in **Figure 2**, venture capital funding of private emerging therapeutic companies reached a decade high of $12.3 billion in 2018. This is a 56% ($4.4 billion) increase from the prior record set in 2017 ($7.9 billion). The top quartile of companies received 72% of all venture funding in 2018. The top three companies raised nearly $1.5 billion combined, and 21 companies raised more than $100 million each. The top 40 companies raised more than 50% of all U.S. venture capital. This illustrates that much of the increase in invested venture dollars went to a small group of companies.

We categorized venture equity investments according to level of novelty. Investments were differentiated as either "novel" drug R&D or drug "improvement" R&D. Novel drug R&D is defined as innovative, unique, and potentially disease-modifying agents for diseases with current unmet medical need. Improvements include new delivery methods, new formulations, or approved drugs for new indications. As seen in **Figure 2**, the majority of venture funding continues to flow into novel drug R&D, with a decade average at 84% of funding, and accounting for 95% of funding in 2018.

With respect to phase of development, early-stage companies continue to receive a large share of venture capital investment. As seen in **Figure 2**, almost half of venture funding in 2018 went into preclinical-stage companies.

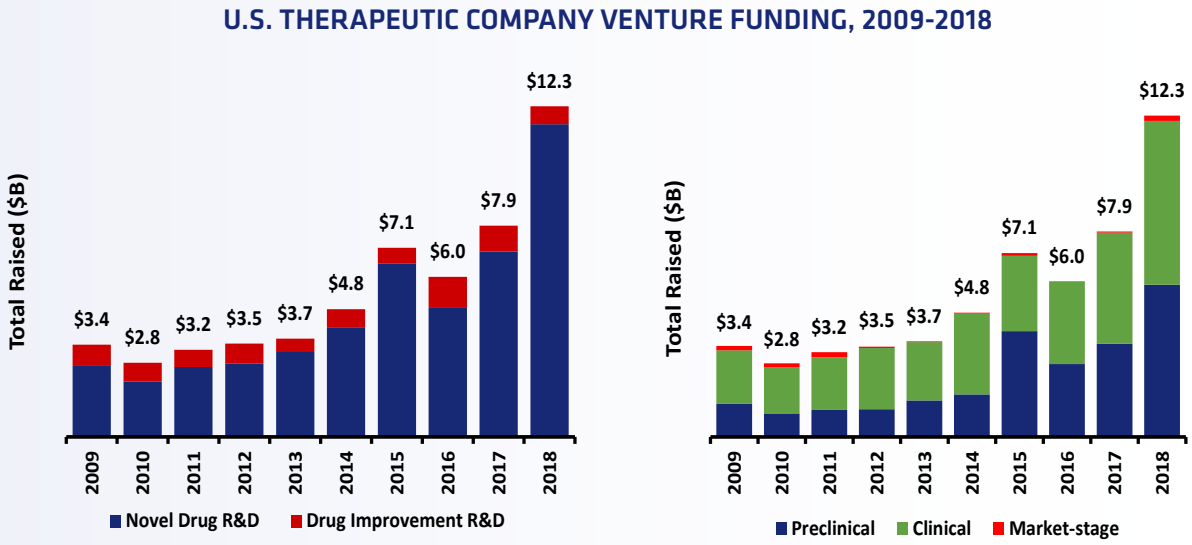


Figure 2. Total venture funding from 2009-2018. Left: Funding is represented as investment toward R&D of novel molecular entities vs. R&D for improvements of approved drugs (including delivery and reformulation). Right: Total venture funding by Phase of Development.

Novel Drug R&D = R&D pursuing new chemical entities to treat disease, with no prior regulatory approval. Drug Improvement R&D = R&D that improves upon existing therapeutics, such as new delivery methods, new formulations, or using approved drugs for new indications. Examples: Drug delivery patch, topical cream, implanted delivery device, needle-less injection, extended release, prolonged half-life chemical modifications (conjugations, including pegylated variants), and reformulations of approved drugs.

As seen in **Figure 3**, the number of companies funded at preclinical-stage is increasing, whereas there is a more stable number of companies at clinical-stage. In 2018, 201 U.S.-based preclinical-stage companies and 136 U.S.-based clinical-stage companies received venture financing. Very few U.S. companies with a product on the market are funded through venture financing.

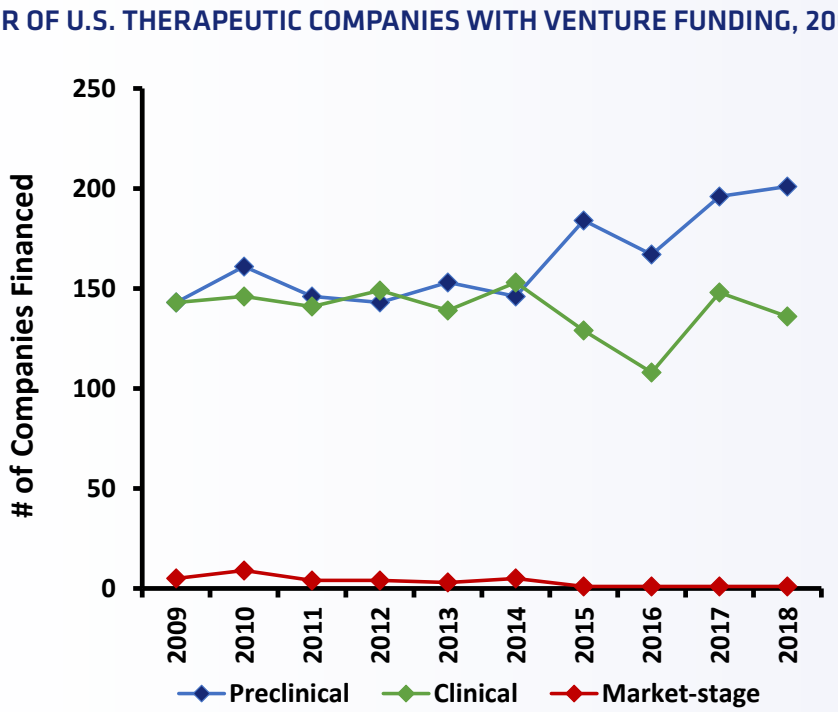


Figure 3. Number of companies with venture investment transactions by development stage, 2009-2018.

The 12 broad disease areas oncology, neurology, infectious, cardiovascular, endocrine, metabolic, ophthalmology, immunology (includes inflammation), respiratory, hematology, gastrointestinal, psychiatry (along with two additional categories: Platform and Other as described under Methods) were analyzed for venture trends over the last decade, as shown in **Figure 4**.

As a percentage of total U.S. venture capital tracked, 36% went into oncology in 2018, an increase from the lows seen in 2010-2012 when it was only 21%. As can be seen in **Figure 4**, the record $4.4 billion in venture financing for oncology towers over the other disease areas, with the next highest funded area, neurology (includes pain), at $1.5 billion. Funding for oncology is up 389% since 2009.

Eight other disease areas, besides oncology and neurology mentioned above, saw increases in 2018. Infectious disease matched a record set in 2015 with $1.4 billion raised across just 19 companies. Endocrine, metabolic, immunology/inflammation, respiratory, hematology, reached decade highs in 2018.

Companies with lead programs in psychiatry, hematology, cardiovascular, and gastrointestinal diseases, as well as platform companies with no announced lead program, saw a decrease in funding in 2018.

Figure 4 includes new delivery, repurposed, and reformulation of already approved products. Removing these company financings would shrink the dollar amounts for areas such as cardiovascular, endocrine, and psychiatry where more reformulation-focused R&D can be found. In the case of psychiatry, one company (which is investigating a new delivery formulation of an already approved product) raised the majority of the dollars in 2018 with a $110 million series B round.

U.S. THERAPEUTIC COMPANY VENTURE FUNDING BY DISEASE, 2009-2018

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	64	64	74	75	64	80	89	95	120	109
Neurology	41	42	40	40	39	35	39	35	46	53
Infectious	37	43	34	20	33	34	30	30	32	19
Other	25	34	19	24	26	27	31	21	37	31
Platform	24	32	24	27	29	40	26	28	18	40
Cardiovascular	15	18	18	16	16	12	12	3	7	11
Endocrine	19	17	18	16	17	12	17	15	19	14
Metabolic	11	11	13	18	13	11	17	10	17	15
Ophthalmology	18	15	15	13	21	15	12	12	14	10
Immunology	14	11	8	12	10	15	11	8	11	14
Respiratory	9	11	10	7	8	8	13	8	10	10
Hematology	6	10	7	11	7	5	7	4	2	1
Gastrointestinal	3	4	4	8	5	4	5	3	7	6
Psychiatry	5	4	6	10	7	6	5	4	5	5
Total (#)	291	316	290	297	295	304	314	276	345	338

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	$919	$616	$923	$740	$1,045	$1,225	$2,011	$1,570	$3,009	$4,434
Neurology	$532	$314	$219	$313	$355	$456	$1,000	$684	$843	$1,452
Platform	$221	$250	$146	$286	$341	$886	$1,020	$512	$450	$1,020
Infectious	$452	$323	$383	$167	$350	$535	$574	$782	$959	$372
Other	$225	$320	$206	$367	$283	$333	$474	$323	$676	$934
Endocrine	$176	$77	$279	$284	$157	$305	$372	$887	$686	$508
Metabolic	$162	$176	$241	$371	$265	$161	$433	$176	$396	$714
Immunology	$157	$152	$57	$148	$171	$262	$260	$332	$194	$737
Cardiovascular	$167	$141	$256	$283	$177	$56	$245	$51	$127	$850
Ophthalmology	$196	$92	$216	$107	$275	$272	$166	$231	$215	$206
Respiratory	$106	$154	$106	$65	$60	$59	$210	$138	$170	$428
Gastrointestinal	$39	$67	$66	$87	$52	$18	$76	$18	$70	$466
Psychiatry	$50	$39	$58	$111	$44	$154	$49	$201	$35	$179
Hematology	$90	$104	$91	$150	$90	$42	$162	$66	$48	$27
Total ($M)	$3,491	$2,826	$3,247	$3,479	$3,665	$4,765	$7,050	$5,970	$7,879	$12,328

Figure 4. Total number of venture capital deals for each disease group (top) as well as the amount invested by disease (bottom) from 2009-2018. Disease categories are sorted by 10-year totals. Data includes novel drug and drug improvement R&D investment.

Series A Venture Funding for U.S. Therapeutic Companies

Series A funding is the first significant financing round after the smaller "Seed" round, and often involves a syndicate of venture firms that back a new approach to drug development. Tracking these rounds allows us to gauge investor appetite for, and commitment to, new early-stage companies.

In 2018, a record amount was raised in Series A rounds, with nearly $5.0 billion going to early-stage companies. Series A has accounted for 33% of all venture investment over the last 10 years and 40% in 2018, indicating a continued shift toward earlier rounds of investment. Almost all Series A funding went into novel drug R&D in 2018, with only 3.3% invested in drug improvement R&D.

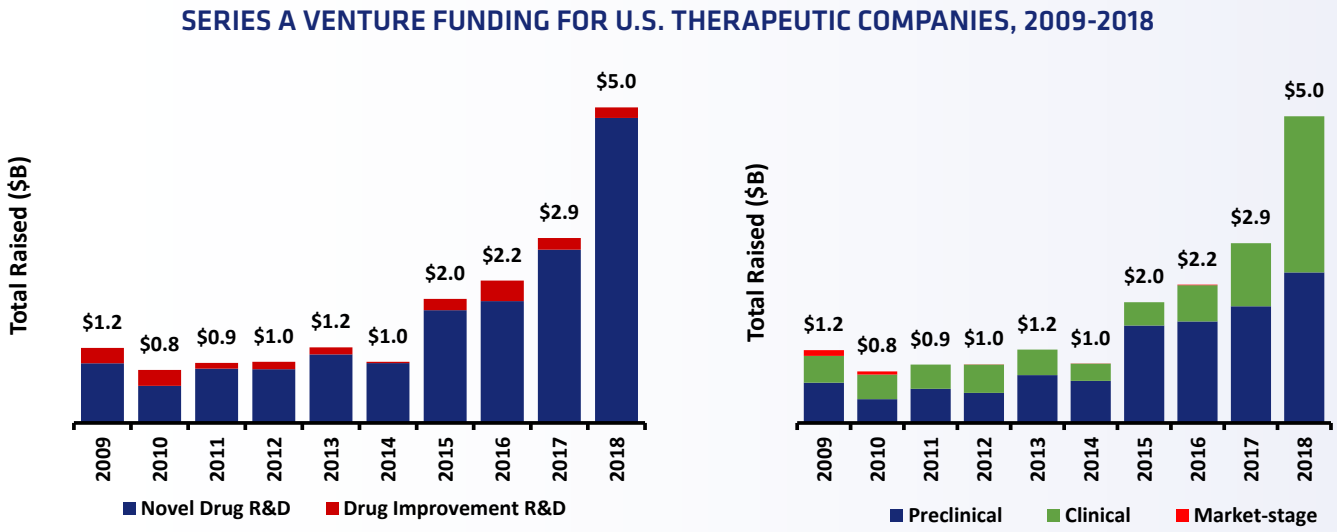


Figure 5. Series A venture funding ($ billions) from 2009-2018. Left: Funding is represented as investment toward R&D of novel molecular entities (blue) vs. improvements of approved drugs (red). Right: Funding is represented by phase at time of financing.

Preclinical companies took in 49% of all Series A venture dollars in 2018, down from 67% in 2017, as seen in **Figure 5**.

Some clinical-stage companies received late tranches of Series A funding, thus not all Series A rounds are truly the first-time financings of funds to propel companies into the clinic. By labeling "first-time" Series A financings in our dataset (A-1 rounds), we were able to track the trends of substantial start-up capital for moving programs into late animal testing or early human trials. As shown in **Figure 6**, the number increased to a record 109 in 2018, beating the previous "ceiling" of around 85-90 that had been reached in multiple years since 2003. Oncology A-1 rounds did not increase from recent averages (29 in 2018 vs. 31 average over the last three years), suggesting a possible shift in the breadth and diversification for start-up U.S. emerging companies. In fact, all of the increases in A-1 financings in 2018 came from neurology and platform companies.

FIRST-TIME SERIES A FUNDING FOR U.S. THERAPEUTIC COMPANIES, 2003-2018

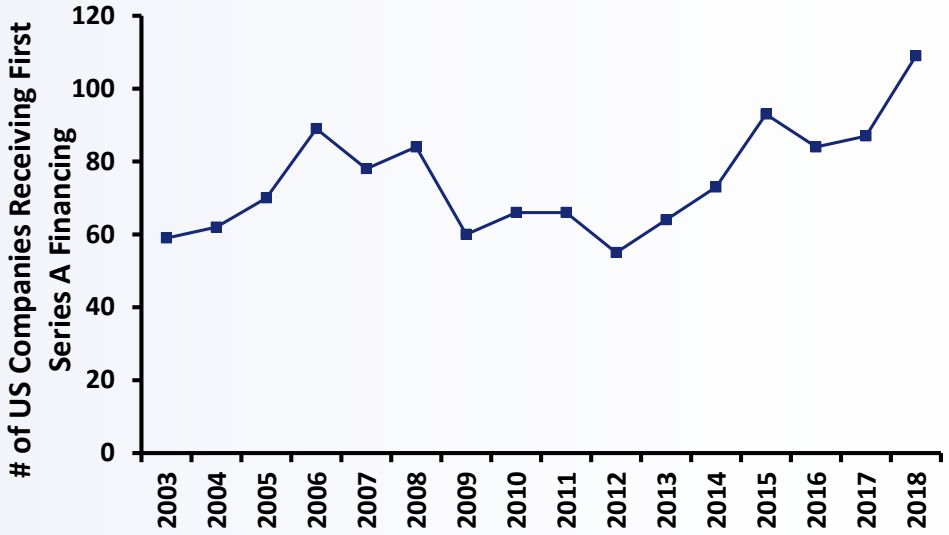


Figure 6. Number of companies receiving their first Series A round (A-1 rounds), 2003-2018.

To investigate trends in all tranches for Series A rounds, we examined the number of companies and amount of Series A funding received by disease category in **Figure 7** below.

Oncology reached record amounts once again in 2018, with $1.4 billion in funding, despite going to fewer companies. More than 50 oncology companies received Series A funding in each of the last three years. This dropped to 43 in 2018, suggesting either larger A rounds on average or a few outliers. Six oncology companies raised more than $50 million, with one company raising over $400 million. Only one other year (2017) had more than three oncology companies raise more than $50 million, 2017 with five. As a percentage of Series A, oncology dropped to 29%, down from the 35-39% range seen in recent years.

As a percentage, platform companies jumped to 17.5% of the 148 Series A financings (all tranches in 2018) from 7% last year. A total 26 platform companies raised $687 million in 2018 (**Figure 7**).

Neurology companies reached a decade high both in terms of companies funded and dollars raised in 2018, with 25 companies receiving $792 million in Series A funding. Another record was set in the "other" category for 2018, with $635 million raised across 15 companies. 91% of this funding was due to a dermatology company raising $438 million and a liver disease company raising $140 million in 2018.

Four disease categories, of the 14 listed in **Figure 7**, raised less than $100 million each in 2018. Companies with lead products in hematology did not raise any funds. Cardiovascular, ophthalmology and psychiatry companies raised $31, $42, and $58 million, respectively. This is 25-45 times lower than oncology Series A funding.

SERIES A VENTURE FUNDING FOR U.S. THERAPEUTIC COMPANIES, BY DISEASE, 2009-2018

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	21	21	30	23	25	29	51	55	57	43
Neurology	21	18	20	19	16	13	16	18	22	25
Platform	11	13	8	10	17	22	14	19	11	26
Other	11	15	9	10	11	10	12	10	15	15
Infectious	12	17	10	9	11	11	15	11	11	9
Endocrine	5	6	8	7	5	4	7	5	9	5
Ophthalmology	6	8	6	7	7	3	3	4	5	3
Cardiovascular	6	8	8	7	6	5	5	1	3	3
Metabolic	4	4	5	6	2	2	7	4	10	4
Immunology	7	3	6	4	2	3	2	3	4	6
Respiratory	3	6	4	1	2	3	2	1	4	4
Hematology	4	5	1	4	3	3	3	4	1	0
Psychiatry	1	2	3	4	4	1	4	3	1	2
Gastrointestinal	2	3	0	2	1	0	2	2	4	3
Total (#)	114	129	118	113	112	109	143	140	157	148

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	$324	$135	$250	$99	$375	$251	$691	$781	$1,037	$1,426
Neurology	$226	$121	$119	$114	$142	$163	$392	$269	$559	$792
Platform	$113	$98	$52	$152	$215	$241	$174	$343	$268	$687
Other	$98	$126	$67	$82	$95	$39	$117	$189	$125	$635
Infectious	$86	$37	$128	$56	$93	$95	$173	$57	$248	$171
Metabolic	$28	$13	$79	$80	$28	$18	$146	$81	$194	$146
Immunology	$115	$16	$50	$51	$10	$44	$9	$63	$41	$410
Ophthalmology	$49	$45	$92	$59	$113	$26	$28	$32	$111	$42
Endocrine	$47	$12	$12	$29	$9	$19	$65	$68	$105	$172
Gastrointestinal	$9	$64	$0	$16	$15	$0	$27	$11	$69	$293
Cardiovascular	$41	$38	$22	$133	$44	$18	$54	$50	$72	$31
Psychiatry	$2	$25	$24	$39	$20	$7	$29	$192	$14	$58
Respiratory	$22	$62	$50	$3	$0	$8	$34	$45	$34	$120
Hematology	$26	$45	$2	$54	$35	$37	$21	$66	$45	$0
Total ($M)	$1,183	$838	$948	$966	$1,193	$965	$1,960	$2,247	$2,922	$4,983

Figure 7. Series A venture funding ($M) and number of venture transactions for U.S. companies by disease area, 2009-2018. Disease categories are sorted by 10-year totals. Data includes novel drug and drug improvement R&D investment.

Venture Capital Funding for Ex-U.S. Emerging Companies

Figure 8 shows the total dollar amount of global venture capital invested in Ex-U.S. emerging companies each year from 2009-2018. Venture funding of ex-U.S. companies has risen every year since 2010, expanding from $1 billion to $5.2 billion in 2018. By contrast, venture funding of U.S. companies has not had consecutive year over year increases, illustrated by the down year in 2016. The totals in **Figure 8** include both novel drug and drug improvement funding. As we saw with venture funding into U.S. companies, funding of Ex-U.S. companies is also more than 90% committed to novel R&D.

Nearly 40% of Ex-U.S. venture funding went to preclinical-stage companies, a level consistent over the past four years but less than the percent seen in the U.S. (49%). Most of the disease categories show an increase in funding for the most recent five-year period.

The regional breakdown of Ex-U.S. venture shows one of the most radical of trend changes in our private investment data. In **Figure 9**, we breakout region and country funding for 2009 and 2018 to illustrate where the Ex-U.S. change has been the greatest. Europe comprised 81% of venture funding of companies outside the U.S. in 2009 and by 2018 only accounted for 41%. As a percentage of total Ex-U.S. venture funding, European countries that saw a decrease since 2009 were Switzerland, Germany, Denmark and Spain. The upward trend of venture funding for Ex-U.S. companies was almost entirely attributed to increased funding of Chinese emerging biotechnology companies, which grew from 1% in 2009 to 47% in 2018 (**Figure 9**).

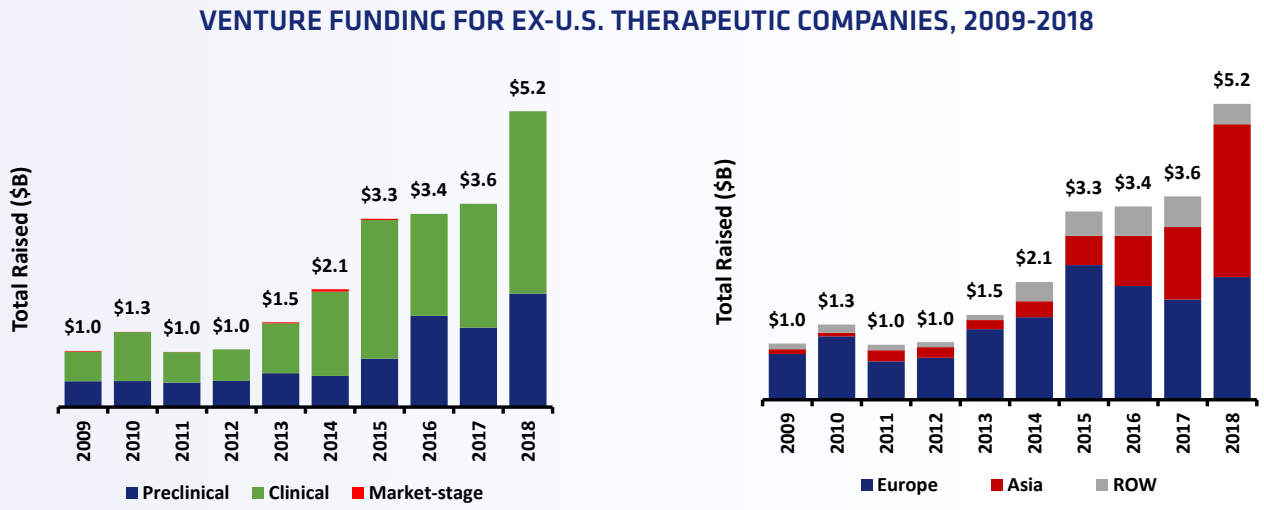


Figure 8. Total venture funding from 2009-2018. Left: Funding is represented as investment toward R&D of novel molecular entities vs. R&D for improvements of approved drugs (including delivery and reformulation). Right: Total venture funding by Phase of Development with the number of companies financed by year.

PRECENTAGE OF VENTURE FUNDING FOR EX-U.S. THERAPEUTIC COMPANIES, 2009 VS 2018

Region	2009	2018
Asia	9%	32%
Europe	81%	60%
ROW	10%	8%

Top 15 Countries 2018	2009	2018
China	1%	47%
United Kingdom	15%	17%
France	3%	5%
Sweden	0%	4%
Bermuda	0%	4%
Belgium	4%	4%
Switzerland	24%	4%
Canada	7%	2%
South Korea	1%	2%
Ireland	5%	2%
Netherlands	4%	2%
Singapore	0%	2%
Germany	8%	1%
Denmark	8%	1%
Spain	4%	1%

Figure 9. Percent of the total amount of venture investment for Ex-U.S. therapeutic companies from 2009 vs. 2018, by region and by country.

NUMBER OF VENTURE FUNDED EX-U.S. THERAPEUTIC COMPANIES, 2009-2018

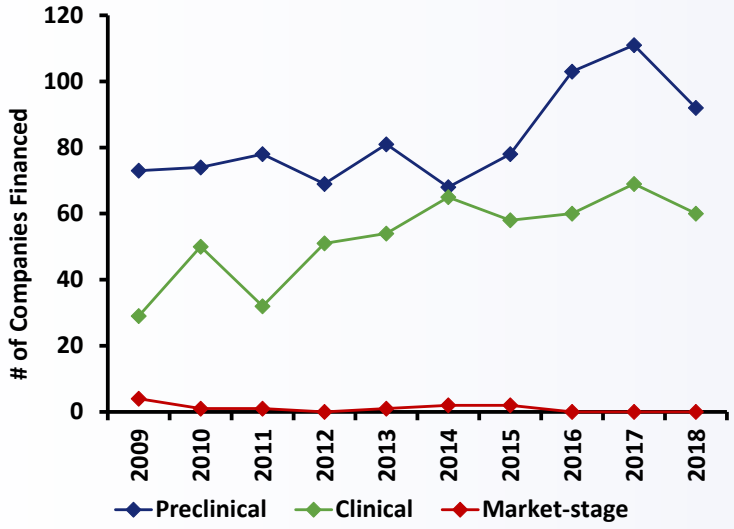


Figure 10. Number of companies that received venture investment by phase, 2009-2018.

Figure 10 shows the number of Ex-U.S. companies venture financed each year, broken out by phase of development. The total number of companies funded grew from 106 in 2009 to a peak of 180 in 2017. In 2018, only 152 companies were funded, the lowest total amount in three years. Unlike with total dollars raised, the number of preclinical-stage companies funded outpaces the number of clinical-stage companies in each of the years analyzed.

The number of Ex-U.S. companies financed, and total raised by lead product disease area can be found in **Figure 11**. As with the U.S. venture funding (and with all areas in this report without exception), Ex-U.S. companies focused on oncology had the highest total amount of dollars raised compared to companies focused on the other 13 disease categories. This holds for total dollars raised as well. Other areas with recent increases are infectious disease, immunology, endocrine, and platform companies.

VENTURE FUNDING FOR EX-U.S. THERAPEUTIC COMPANIES BY DISEASE, 2009-2018

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	18	31	27	33	33	36	41	52	57	48
Infectious	19	19	15	14	18	14	18	18	23	18
Platform	13	20	14	11	16	12	10	16	18	24
Neurology	14	9	10	16	19	14	13	12	12	12
Other	11	10	15	11	17	16	12	12	14	7
Immunology	12	9	8	10	9	4	1	13	8	14
Endocrine	5	8	5	5	3	9	6	6	7	6
Cardiovascular	4	6	3	3	7	7	8	7	8	5
Ophthalmology	4	3	7	4	4	7	11	9	5	3
Metabolic	1	3	3	2	3	3	6	1	10	6
Gastroinstestinal	2	1	0	4	2	4	3	10	6	3
Respiratory	2	3	1	5	2	3	3	4	4	2
Hematology	1	2	2	1	1	3	3	0	5	3
Psychiatry	0	1	1	1	2	3	3	3	3	1
Total (#)	106	125	111	120	136	135	138	163	180	152

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	$134	$312	$225	$382	$471	$820	$1,666	$1,453	$1,310	$2,292
Infectious	$153	$189	$63	$75	$158	$99	$350	$317	$428	$535
Platform	$75	$135	$120	$83	$170	$145	$131	$605	$305	$371
Immunology	$133	$58	$65	$53	$145	$16	$21	$188	$249	$622
Other	$74	$59	$234	$122	$210	$175	$258	$115	$151	$108
Neurology	$160	$202	$52	$138	$140	$195	$181	$125	$137	$173
Endocrine	$57	$156	$61	$49	$16	$107	$157	$93	$114	$443
Cardiovascular	$23	$110	$17	$5	$45	$122	$124	$185	$272	$129
Gastroinstestinal	$75	$21	$0	$25	$15	$83	$18	$164	$208	$110
Ophthalmology	$46	$5	$52	$3	$62	$58	$164	$74	$124	$38
Metabolic	$15	$17	$30	$34	$19	$67	$141	$0	$98	$93
Respiratory	$28	$33	$5	$19	$24	$48	$9	$5	$136	$132
Hematology	$11	$18	$23	$24	$4	$101	$51	$0	$32	$140
Psychiatry	$0	$4	$19	$1	$8	$30	$34	$68	$5	$4
Total ($M)	$986	$1,320	$966	$1,011	$1,487	$2,067	$3,304	$3,391	$3,569	$5,190

Figure 11. Total number of venture capital deals for each disease group as well as the amount invested by disease from 2009-2018. Disease categories are sorted by 10-year totals. Data includes novel drug and drug improvement R&D investment.

Series A Venture Funding for Ex-U.S. Therapeutic Companies

In 2018, a record amount of Series A funding went to Ex-U.S. therapeutic companies, narrowly edging the previous record set in 2016 by 6% (**Figure 12**). There has been a 600% increase in series A funding provided to Ex-U.S. emerging therapeutic companies over the past decade - increasing from $0.2 billion in 2009 to $1.5 billion in 2018. The majority of this funding was for preclinical-stage companies, with clinical-stage companies only receiving 26% of the total Series A funding in recent years.

The regional shift in Series A funding for Ex-U.S. therapeutic companies mirrors the dramatic shift seen in the combined finance data discussed in the previous section. In 2018 European companies received 36% of Series A funding while Asian companies accounted for 60% of all Series A funding given to Ex-U.S. companies. There was a noticeable spike in the ROW category in 2016 that can be attributed to a single Canadian company that raised $225 million.

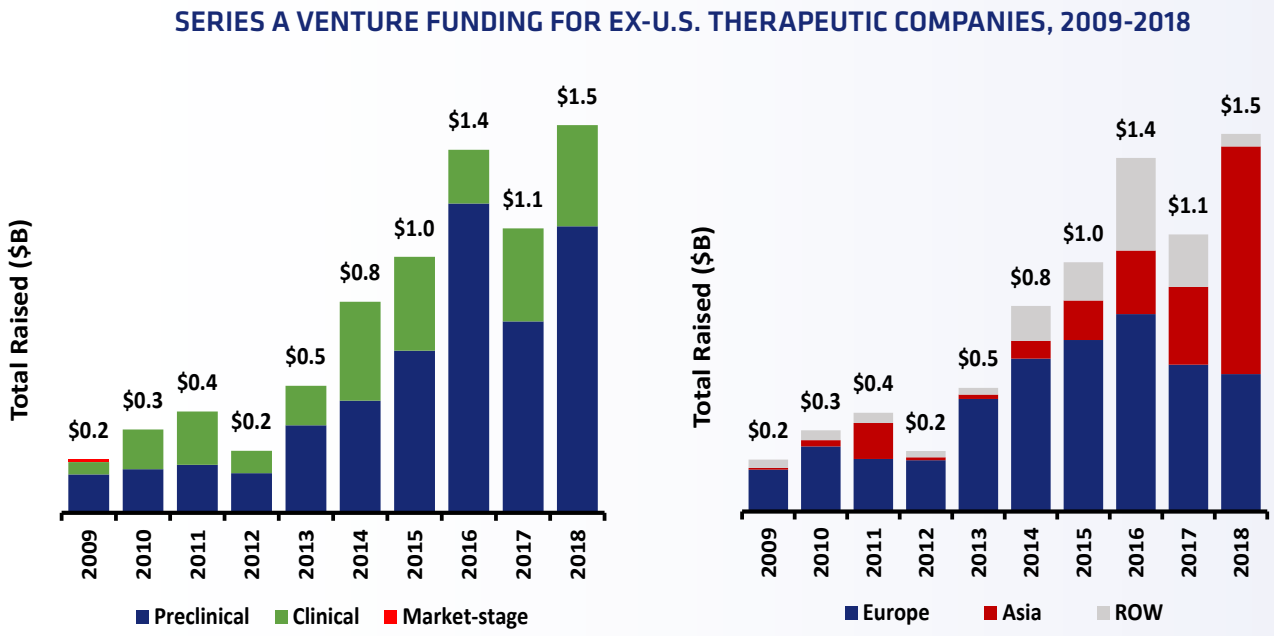


Figure 12. Series A venture funding ($M) from 2009-2018. Left: Funding is represented as investment toward R&D of novel molecular entities (blue) vs. improvements of approved drugs (red). Right: Funding is represented by phase at time of financing.

Interestingly, the number of "first-time" Series A financings (A-1 rounds) for Ex-U.S. therapeutic companies decreased in 2018 for the second year in a row. As shown in **Figure 13**, the number of A-1 rounds approached 60 in 2016 but dropped below 50 in 2018. This is not consistent with the trend we observed with U.S. companies. Upon closer examination we found that there were multiple outliers with above normal Series A dollars going to several Chinese companies, some well above $100 million. The 10-year average Series A round for an Ex-U.S. company is $13 million.

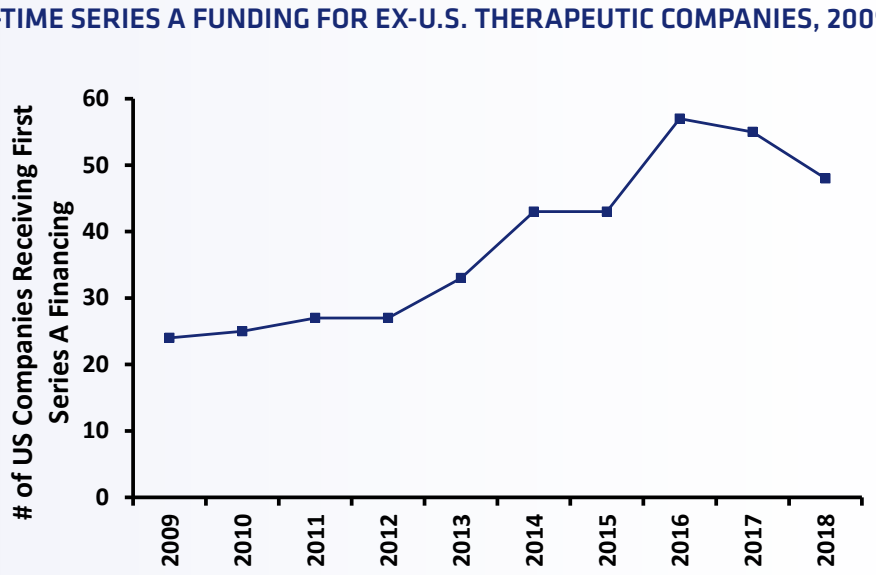


Figure 13. Number of Ex-U.S. therapeutic companies receiving their first Series A round (A-1 rounds), 2009-2018.

When we delineated companies by disease area focus, we found that 22 oncology companies obtained $684 million from Series A rounds in 2018 (**Figure 14**). This amount represents 36% of all Series A financing for Ex-U.S. therapeutic companies.

A significant increase in Series A funding was found for Ex-U.S. companies working on infectious diseases in 2018. Four infectious disease companies raised $332 million, compared to only $107 million for nine companies in 2017.

We did not find any Series A stage financing for Ex-U.S. companies focused on metabolic and endocrine diseases. Three disease areas, psychiatry, gastrointestinal, and ophthalmology, each had only one company obtaining Series A funding in 2018.

SERIES A FUNDING FOR EX-U.S. THERAPEUTIC COMPANIES BY DISEASE, 2009-2018

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	8	8	9	13	12	14	18	26	22	22
Other	5	9	4	4	4	9	3	9	10	13
Platform	7	3	6	1	7	7	10	5	6	6
Infectious	3	3	7	4	9	5	5	6	9	4
Neurology	4	5	4	7	6	7	6	3	5	4
Cardiovascular	3	4	2	5	2	0	0	9	3	3
Endocrine	1	0	3	1	2	5	5	6	0	0
Respiratory	1	2	2	2	0	5	2	0	4	2
Ophthalmology	0	1	2	1	3	4	2	2	2	1
Immunology	0	1	0	0	1	2	3	0	5	3
Metabolic	1	0	1	3	0	2	2	1	1	0
Psychiatry	1	0	0	2	1	0	1	3	2	1
Gastroinstestinal	0	0	1	0	2	0	1	1	2	1
Hematology	0	1	1	0	0	0	1	0	2	2
Total (#)	34	37	42	43	49	60	59	71	73	62

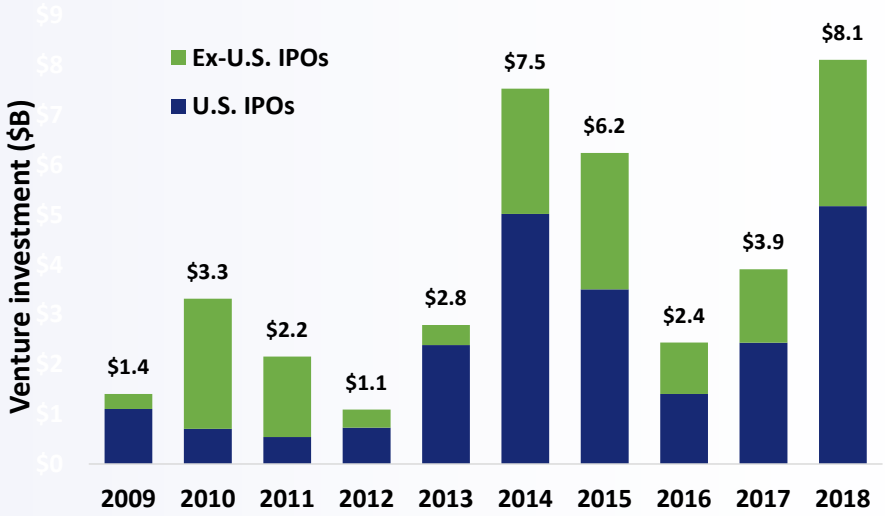
Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	$51	$41	$96	$93	$131	$328	$252	$629	$275	$684
Platform	$52	$81	$20	$27	$38	$89	$42	$350	$220	$138
Infectious	$38	$17	$35	$0	$67	$45	$161	$87	$107	$334
Other	$16	$16	$51	$42	$95	$30	$129	$37	$81	$85
Neurology	$7	$67	$20	$24	$35	$62	$57	$9	$27	$88
Cardiovascular	$0	$30	$16	$3	$28	$108	$57	$12	$105	$5
Endocrine	$1	$21	$54	$16	$0	$28	$126	$0	$81	$13
Immunology	$18	$22	$20	$14	$13	$0	$0	$133	$67	$47
Ophthalmology	$0	$0	$39	$0	$43	$57	$31	$71	$0	$0
Metabolic	$0	$8	$0	$0	$18	$27	$57	$0	$54	$65
Gastroinstestinal	$20	$0	$0	$5	$12	$0	$14	$24	$36	$8
Hematology	$0	$17	$12	$0	$0	$0	$37	$0	$28	$16
Psychiatry	$0	$0	$19	$0	$8	$0	$9	$36	$5	$4
Respiratory	$1	$0	$5	$14	$0	$36	$9	$5	$5	$0
Total ($M)	$205	$320	$389	$238	$487	$809	$981	$1,392	$1,091	$1,486

Figure 14. Series A venture funding ($M) and number of venture transactions for Ex-U.S. companies by disease area, 2009-2018. Disease categories are sorted by 10-year totals. Data includes novel drug and drug improvement R&D investment.

Initial Public Offerings

Global IPOs from emerging therapeutic companies increased significantly in 2018. A total 77 IPOs from small drug developers around the world (at all phases of drug development) raised $8.1 billion, a record high. Most of this increase can be attributed to the U.S. and Asia (**Figure 15**). Europe however, dropped from 19 IPOs in 2017 to 8 last year with the same amount of dollars raised in both years ($800 million). Over the last six years, the level of investment has been volatile, with 2013 and 2016 below $3 billion and 2014 and 2018 above $7 billion.

IPOS FOR EMERGING THERAPEUTIC COMPANIES WORLDWIDE, 2009-2018



# IPOs	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
USA	3	12	8	11	32	58	39	22	25	49
Europe	1	7	4	4	6	20	33	14	19	8
Asia	4	7	11	7	5	7	10	12	8	17
ROW	2	1	1	0	1	9	1	0	3	3
Global	10	27	24	22	44	94	83	48	55	77

$B Raised	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
USA	$1.1	$0.7	$0.5	$0.7	$2.4	$5.0	$3.5	$1.4	$2.4	$5.2
Europe	$0.2	$0.2	$0.1	$0.1	$0.2	$1.3	$1.3	$0.4	$0.8	$0.8
Asia	$0.1	$2.4	$1.5	$0.3	$0.2	$0.8	$1.4	$0.6	$0.4	$1.9
ROW	$0.1	$0.0	$0.0	$0.0	$0.0	$0.4	$0.0	$0.0	$0.2	$0.2
Global	$1.4	$3.3	$2.2	$1.1	$2.8	$7.5	$6.2	$2.4	$3.9	$8.1

Figure 15. IPOs for global emerging therapeutic companies, 2009-2018. Includes emerging companies at market-stage with less than $1 billion in product sales. Amount raised ($ billions) and number of deals by region. See Appendix for countries included in Europe, Asia, and rest of world (ROW).

Initial Public Offerings for U.S. R&D-Stage Companies

The number of IPOs for U.S. R&D-stage companies almost doubled from 24 in 2017 to 47 in 2018, (**Figure 16**). Although this is not greater than the record high reached in 2014 (55 IPOs), the total amount raised did set a record (U.S. R&D-stage raised $5.1 billion vs previous high of $4 billion in 2014).

Nearly absent from 2017 IPOs, U.S. preclinical-stage companies returned to the public market offerings list in 2018 with nine companies raising $1 billion. Clinical-stage U.S. company IPOs increased from 23 to 38 in 2018, hitting a four-year high. Phase I and Phase II stage companies raised $4 billion combined, setting a record for both stages of development.

The average amount raised per IPO for R&D-stage companies was $108 million in 2018, the highest amount seen over the past decade. The stock market was strong in the first nine months of 2018 when most of the IPOs took place, with clinical-stage biotechs up 21% for the year by September 30th. The last quarter of 2018 was volatile, with clinical-stage companies dropping 32% in the fourth quarter. However, 12 companies were able to launch IPOs during the 4th quarter, including the largest IPO in biotech history which raised over $600 million.

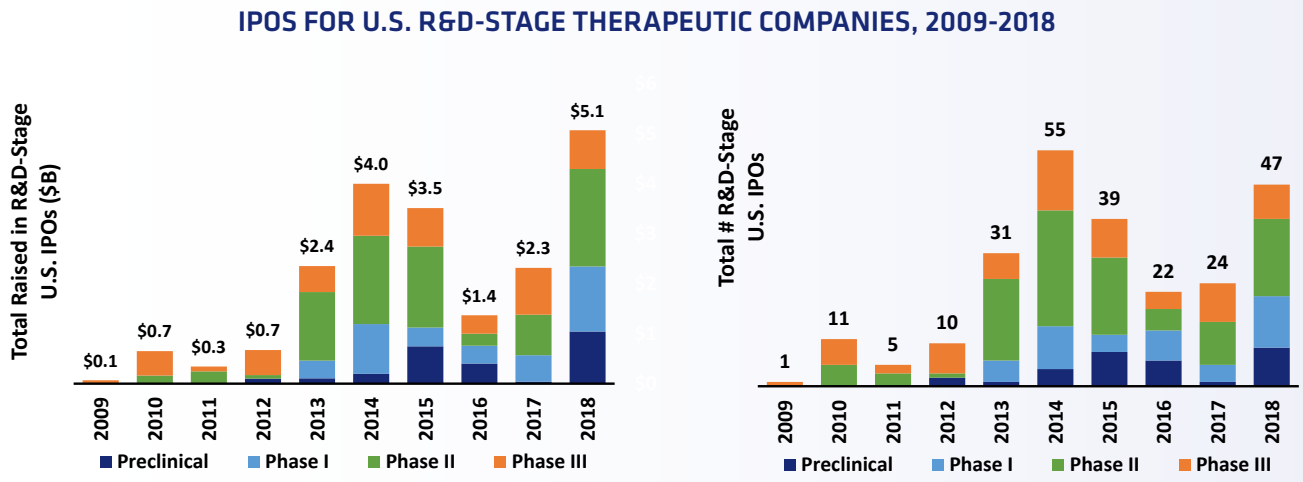


Figure 16. Left: IPOs for U.S. R&D-stage therapeutic companies, by phase, 2009-2018. Right: The number of IPOs and total dollars raised via IPOs per year for R&D-stage and market-stage companies.

Figure 17 shows the last decade of U.S. R&D-stage IPOs by company's lead disease area. In 2018, a record number of oncology (14), metabolic (7), ophthalmology (4), and inflammation (4) IPOs were completed. In terms of dollars raised, R&D-stage oncology companies stand out with $1.5 billion raised vs. all other areas that each raised less than $1 billion in 2018. The increase in cardiovascular is largely due to how we annotate the data – Moderna's lead compound is in cardiovascular although they actually have numerous other disease categories in their expansive pipeline. Metabolic IPOs jumped from the $160 to $886 million in large part due to rare metabolic disease companies.

IPOS FOR U.S. R&D-STAGE THERAPEUTIC COMPANIES, BY DISEASE, 2009-2018

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	0	1	3	3	13	10	9	4	8	14
Neurology	1	1	1	0	0	7	11	0	3	3
Infectious	0	3	0	2	4	8	2	2	2	2
Metabolic	0	0	0	1	3	2	3	3	2	7
Other	0	1	0	1	0	5	2	2	3	6
Cardiovascular	0	2	0	0	2	3	3	2	2	2
Ophthalmology	0	1	0	0	2	2	2	1	2	4
Endocrine	0	0	0	0	0	8	2	0	0	3
Inflammation	0	1	0	2	1	2	0	1	0	4
Hematology	0	0	0	0	3	3	2	0	1	0
Gastroinstestinal	0	1	1	0	1	1	0	2	0	0
Platform	0	0	0	1	1	1	0	3	0	0
Psychiatry	0	0	0	0	0	1	2	0	1	1
Respiratory	0	0	0	0	1	0	1	1	0	1
Total	1	11	5	10	31	53	39	21	24	47

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	$0	$81	$248	$236	$921	$1,033	$897	$162	$766	$1,518
Neurology	$68	$50	$40	$0	$0	$419	$1,058	$0	$358	$202
Metabolic	$0	$0	$0	$50	$301	$176	$155	$189	$160	$886
Other	$0	$30	$0	$81	$0	$341	$215	$263	$215	$769
Cardiovascular	$0	$90	$0	$0	$134	$161	$253	$91	$215	$650
Infectious	$0	$123	$0	$140	$315	$420	$211	$103	$117	$111
Ophthalmology	$0	$72	$0	$0	$234	$152	$201	$50	$240	$214
Endocrine	$0	$0	$0	$0	$0	$612	$152	$0	$0	$253
Hematology	$0	$0	$0	$0	$205	$309	$192	$0	$75	$0
Inflammation	$0	$17	$0	$120	$73	$92	$0	$70	$0	$332
Gastroinstestinal	$0	$188	$55	$0	$25	$60	$0	$95	$0	$0
Platform	$0	$0	$0	$45	$70	$50	$0	$258	$0	$0
Respiratory	$0	$0	$0	$0	$72	$0	$77	$50	$0	$122
Psychiatry	$0	$0	$0	$0	$0	$33	$98	$0	$168	$7
Total	$68	$650	$343	$672	$2,350	$3,858	$3,508	$1,331	$2,314	$5,064

Figure 17. IPOs for U.S. emerging companies, 2009-2018. Amount raised ($M) and number of deals by disease. Disease categories are sorted by 10-year totals. Data includes novel drug and drug improvement R&D investment.

Initial Public Offerings for Ex-U.S. R&D-Stage Companies

Ex-U.S. R&D-stage IPOs have grown significantly over the decade, from below 10 per year 2009-2012 to more than 20 for each of the last five years, 2014-2018.

2018 showed a slight decrease in the number of transactions, with 22 initial public offerings (IPOs) versus the 24 seen in 2017. Although the number of companies did not increase, the amount raised increased dramatically to $2.3 billion in 2018 versus $1.3 billion in 2017. Of the $2.3 billion raised, 86 percent of the money was invested in late-stage companies (Phase II & III). This is slightly less than 2017, where 92 percent of the IPO investments were in late stage development companies.

The average amount raised per IPO for Ex-U.S. R&D-stage companies was $106 million in 2018, which is more than three times higher compared to the $34 million average during 2008-2017. The observed increase in 2018 IPO financing dollars can largely be attributed to four late-stage Chinese companies that each raised over $100 million, with two raising more than $400 million each.

IPOS FOR EX-U.S. R&D-STAGE THERAPEUTIC COMPANIES, 2009-2018

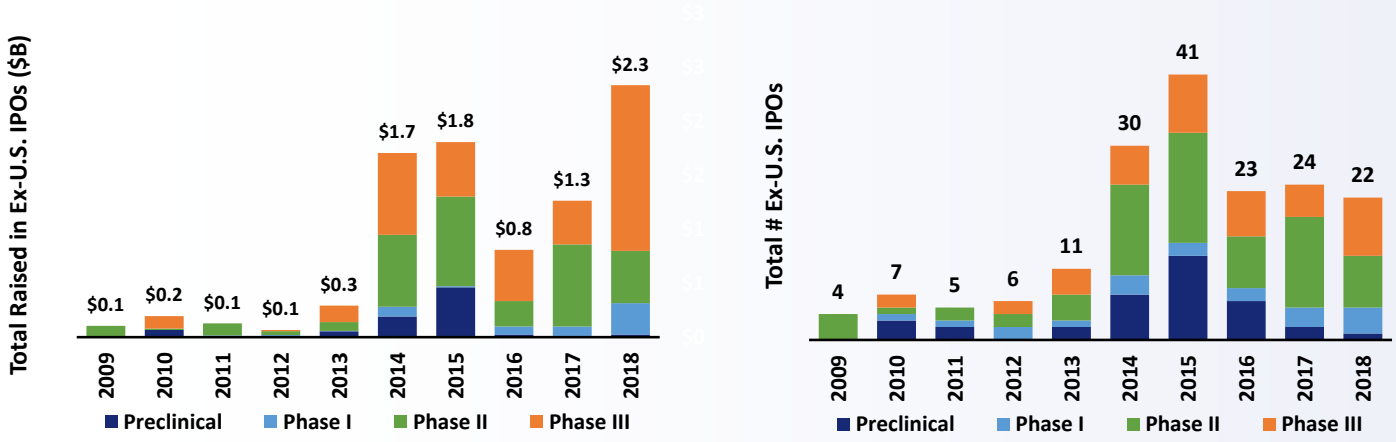


Figure 18. IPOs for Ex-U.S. emerging companies, 2009-2018. Left: Amount raised in $ billion USD, by phase. Right: number of deals by phase.

Many gaps remain for Ex-U.S. public offerings in terms of disease areas funded (**Figure 19**). Ex-U.S. companies with lead programs in respiratory, gastrointestinal, hematology, and psychiatry have not had an IPO in two years. Recent activity is largely attributed to companies focused on oncology, neurology and infectious disease. Oncology funding dwarfs all other areas with at least 4 times the amount raised to as high as 50 times more raised than other diseases in 2018.

IPOS FOR EX-U.S. R&D-STAGE THERAPEUTIC COMPANIES, BY DISEASE, 2009-2018

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	1	1	4	4	3	6	11	7	10	9
Other	0	0	0	0	0	8	4	2	4	3
Neurology	1	0	0	0	2	2	5	4	4	2
Infectious	0	3	0	1	1	1	6	1	1	3
Endocrine	0	1	0	1	0	1	4	1	1	2
Inflammation	1	1	0	0	0	3	3	1	0	1
Cardiovascular	0	0	1	0	2	0	2	1	1	1
Ophthalmology	1	0	0	0	0	3	1	2	1	0
Metabolic	0	0	0	0	1	2	1	1	2	0
Platform	0	1	0	0	1	1	1	0	0	1
Gastroinstestinal	0	0	0	0	0	2	0	1	0	0
Hematology	0	0	0	0	0	0	2	1	0	0
Respiratory	0	0	0	0	0	1	1	1	0	0
Psychiatry	0	0	0	0	1	1	0	0	0	0
Total (#)	4	7	5	6	11	31	41	23	24	22

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	$15	$36	$114	$28	$34	$219	$600	$380	$636	$1,293
Other	$0	$0	$0	$0	$0	$551	$264	$31	$116	$161
Infectious	$0	$29	$0	$2	$47	$36	$285	$33	$20	$320
Neurology	$74	$0	$0	$0	$26	$75	$168	$154	$216	$59
Endocrine	$0	$79	$0	$36	$0	$44	$201	$16	$52	$125
Inflammation	$7	$13	$0	$0	$0	$289	$33	$4	$0	$200
Ophthalmology	$10	$0	$0	$0	$0	$291	$11	$52	$75	$0
Metabolic	$0	$0	$0	$0	$78	$71	$23	$53	$144	$0
Cardiovascular	$0	$0	$14	$0	$31	$0	$157	$3	$6	$153
Platform	$0	$39	$0	$0	$52	$17	$60	$0	$0	$25
Respiratory	$0	$0	$0	$0	$0	$98	$3	$8	$0	$0
Gastroinstestinal	$0	$0	$0	$0	$0	$34	$0	$29	$0	$0
Hematology	$0	$0	$0	$0	$0	$0	$3	$47	$0	$0
Psychiatry	$0	$0	$0	$0	$25	$3	$0	$0	$0	$0
Total ($M)	$106	$196	$128	$67	$293	$1,727	$1,808	$810	$1,264	$2,335

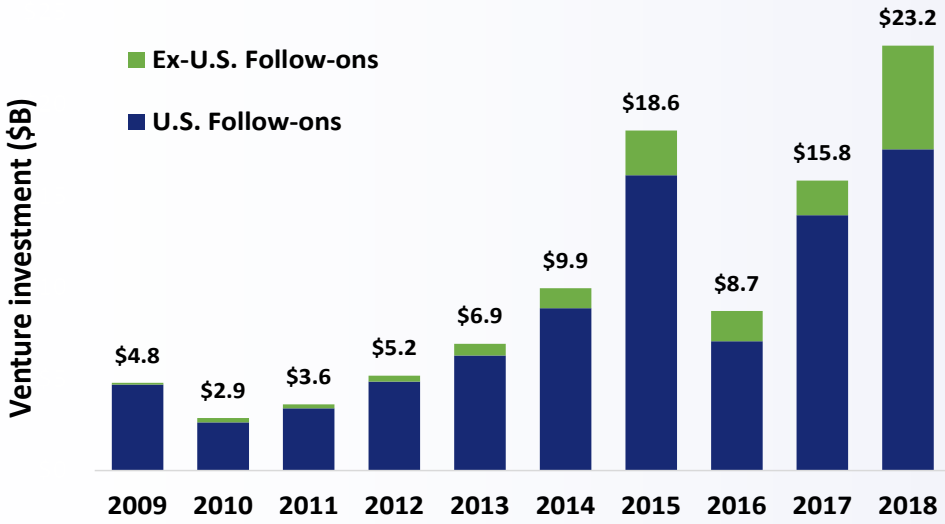
Figure 19. IPOs by R&D-stage Ex-U.S. emerging companies, 2009-2018. Amount raised ($M) and number of deals by disease. Disease categories are sorted by 10-year totals. Data includes novel drug and drug improvement R&D investment.

Follow-On Public Offerings

Follow-on public financing (FOPOs) for global emerging therapeutic companies reached an all-time high in both dollars raised ($23.2 billion) and number of transactions (202) in 2018. U.S. emerging companies accounted for the majority of the increase in terms of both numbers (58%) and amount of capital raised (49%).

Unlike what we saw in the IPO market, European companies rebounded in 2018 reaching a record 22 FOPOs raising $3 billion with 22 transactions. Asian companies experienced their largest year in 2018 with $2 billion raised. This is a significant upward trend as prior to 2016, Asian companies raised less than $0.1 billion each year.

FOLLOW-ON OFFERINGS FOR EMERGING THERAPEUTIC COMPANIES WORLDWIDE, 2009-2018



# Follow-Ons	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
USA	42	45	51	76	89	99	132	87	126	160
Europe	3	1	2	2	5	7	13	8	9	22
Asia	0	1	0	0	1	1	1	2	2	7
ROW	1	3	3	8	7	10	5	13	7	13
Global	46	50	56	86	102	117	151	110	144	202

$B Raised	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
USA	$4.7	$2.6	$3.4	$4.8	$6.3	$8.9	$16.1	$7.1	$13.9	$17.5
Europe	$0.1	$0.1	$0.1	$0.1	$0.3	$0.7	$2.1	$0.7	$1.2	$3.0
Asia	$0.0	$0.1	$0.0	$0.0	$0.1	$0.0	$0.1	$0.3	$0.5	$2.0
ROW	$0.0	$0.1	$0.1	$0.3	$0.2	$0.4	$0.3	$0.7	$0.2	$0.6
Global	$4.8	$2.9	$3.6	$5.2	$6.9	$9.9	$18.6	$8.7	$15.8	$23.2

Figure 20. FOPOs for global emerging therapeutic companies, 2009-2018. indicates the proportion of total dollars raised. Includes only transactions raising over $10 million. Global R&D-stage IPOs from emerging companies, 2009-2018. Amount raised ($B) and number of deals by region. See Appendix for countries included in Europe, Asia, and rest of world (ROW).

Follow-On Public Offerings for U.S. R&D-Stage Companies

Capital raised via FOPOs decreased in 2018 for R&D-stage U.S. emerging companies (**Figure 21**), suggesting that the increase of overall FOPO capital raised by the biopharmaceutical industry (**Figure 20**) was due to market-stage emerging biotechs. However, the decrease of $1 billion was complemented with an all-time high in the number of FOPO financings (118) from U.S. R&D-stage companies. A possible explanation for the decrease in dollars but increase in number of transactions is the increase of both Phase I and Phase II transactions, which increased by 5 and 10 transaction respectively, which have a lower average of capital raised per transaction than those for companies with trials in Phase III [Phase I FOPOs averaged $48 million per transaction, Phase II $89 million per transaction, and Phase III $117 million per transaction.]

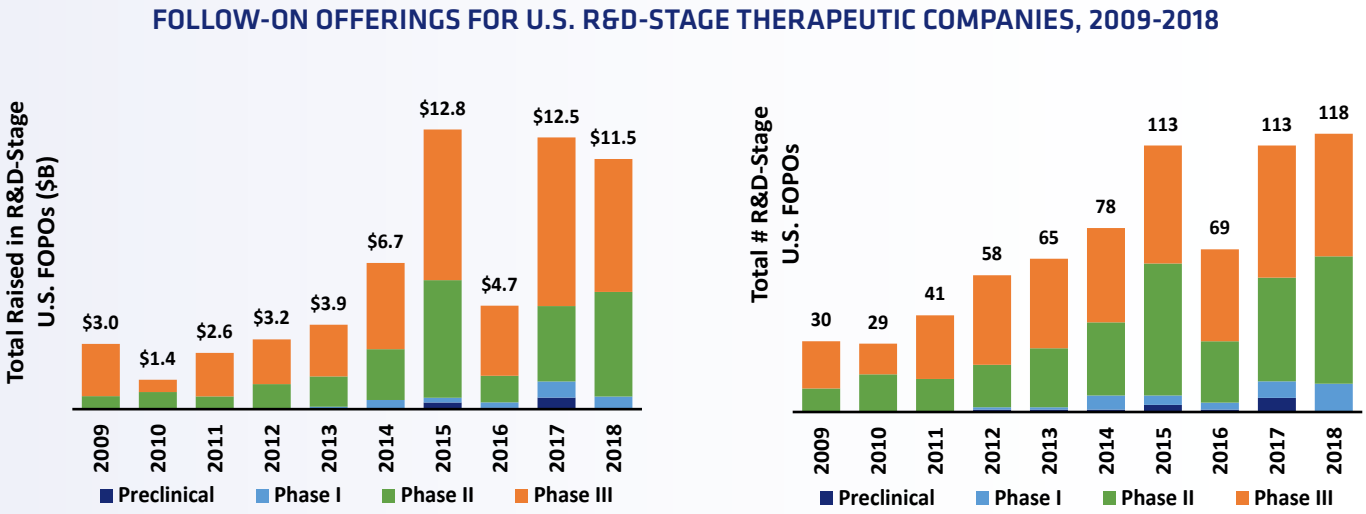


Figure 21. Left: FOPOs for U.S. R&D-stage therapeutic companies, 2009-2018. Right: The number of FOPOs (with values above $10M) and total FOPO dollars raised per year for R&D-stage and market-stage companies, 2008-2017.

U.S. R&D-stage oncology companies continued to raise the most capital through FOPOs ($3.48 billion) and had the most transactions (39) in 2018 vs. other disease groups, as they have consistently done over the last 10 years (**Figure 22**).

Over the past two years we have seen a large shift in the number and dollars raised via FOPOs for hematology companies. In terms of dollars, the majority can be contributed to one gene therapy company that raised $1.1 billion in 2017 and $633 million in 2018. Another outlier in 2018 is in psychiatry, with one company raising $661 million—the largest U.S. R&D stage FOPO transaction of the year.

FOLLOW-ON OFFERINGS FOR U.S. R&D-STAGE COMPANIES, BY DISEASE, 2009-2018

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	13	11	18	27	20	25	35	20	34	39
Infectious	4	8	7	6	13	8	16	6	13	12
Neurology	2	4	2	6	9	9	12	11	9	7
Other	0	0	1	0	5	6	8	9	9	10
Metabolic	3	0	3	5	1	7	8	3	8	9
Endocrine	1	2	3	3	6	5	12	4	3	6
Hematology	1	0	2	1	4	5	2	4	10	10
Immunology	4	0	1	1	2	2	10	2	9	7
Cardiovascular	0	3	2	2	1	6	3	1	5	5
Ophthalmology	0	0	0	3	0	3	6	4	4	4
Gastrointestinal	1	1	2	3	2	0	0	1	2	4
Respiratory	1	0	0	0	2	2	0	1	2	3
Psychiatry	0	0	0	1	0	0	1	3	3	2
Platform	0	0	0	0	0	0	0	0	2	0
Total (#)	30	29	41	58	65	78	113	69	113	118

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	$1,348	$644	$1,466	$1,714	$1,492	$1,751	$2,942	$1,403	$3,409	$3,480
Metabolic	$173	$0	$170	$413	$185	$831	$2,316	$91	$1,880	$1,295
Infectious	$922	$351	$460	$232	$732	$727	$1,663	$311	$1,011	$522
Neurology	$69	$133	$96	$251	$265	$1,314	$1,436	$1,171	$599	$339
Hematology	$86	$0	$63	$18	$203	$403	$115	$460	$1,874	$1,618
Other	$0	$0	$23	$0	$351	$517	$929	$401	$1,178	$752
Endocrine	$62	$36	$87	$205	$255	$255	$1,341	$239	$105	$726
Immunology	$244	$0	$58	$38	$106	$249	$1,215	$141	$556	$583
Cardiovascular	$0	$76	$91	$74	$23	$345	$386	$66	$622	$541
Ophthalmology	$0	$0	$0	$63	$0	$169	$358	$261	$518	$303
Psychiatry	$0	$0	$0	$22	$0	$0	$130	$44	$405	$678
Gastrointestinal	$57	$111	$69	$172	$159	$0	$0	$86	$67	$499
Respiratory	$34	$0	$0	$0	$106	$150	$0	$75	$89	$148
Platform	$0	$0	$0	$0	$0	$0	$0	$0	$155	$0
Total ($M)	$2,996	$1,352	$2,583	$3,202	$3,876	$6,710	$12,831	$4,748	$12,467	$11,483

Figure 22. Follow-On Offerings for U.S. R&D-stage companies by diseases, 2009-2018. Amount raised ($M) and number of deals by disease. Disease categories are sorted by 10-year totals. Data includes novel drug and drug improvement R&D investment.

Follow-On Public Offerings for Ex-U.S. R&D-Stage Companies

Capital raised via FOPOs more than tripled in 2018 for Ex-U.S. R&D-stage companies with $3.2 billion, compared to the $1 billion raised in 2017. This is more money raised in 2018 than the amount seen between 2009-2016 combined. This increase was driven by R&D-stage companies in Europe receiving an increase of $1.8 billion and Asian companies receiving an increase of $1.5 billion in 2018 over 2017.

In 2018, Phase III Ex-U.S. companies raised the highest amount seen over the 10-year period with $2 billion. Phase III companies experience the largest increase both in terms of the number of transactions, with an increase of 7 transactions, and in dollars raised with an increase of $1.4 billion. Ex-U.S.

Companies in the ROW category saw an increase both in terms of dollars and transactions in 2018 compared to 2017 ($631 million raised by 13 transactions). However, these numbers are on par with the amount of dollars raised and number of transactions seen in 2016 ($682 million raised in 13 transactions).

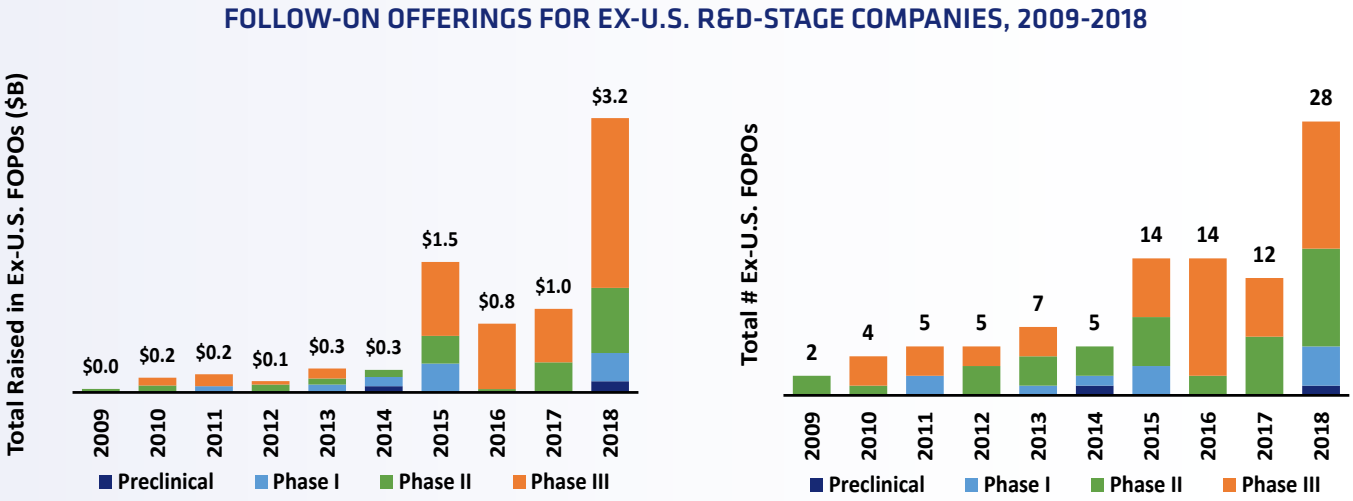


Figure 23. Left: FOPOs for Ex-U.S. R&D-stage therapeutic companies, 2009-2018. Right: The number of FOPOs (with values above $10M) and total FOPO dollars raised per year for R&D-stage and market-stage companies, 2008-2017. (Not shown: Market-stage Ex-U.S. companies raised the highest amount of any other stage in 2018 with $2.4 billion raised by 14 transactions.)

The majority of the disease groups showed a marked increase in the amount of FOPO financing received from 2017 to 2018 (**Figure 24**). Only one disease group, infectious diseases, saw a decrease in FOPO funding in 2018 compared to 2017 ($90 million to $50 million). There were no transactions in 2018 for Ex-U.S. companies focused on respiratory, psychiatry, gastrointestinal diseases and platform technologies. In fact, companies focused on treatments for psychiatry, gastrointestinal, or on platform technologies have not had any FOPO transactions in the past decade. Oncology focused Ex-U.S. companies experienced the largest uptick both in terms of the number of transaction and dollars raised in 2018. One Chinese company raised the two largest transactions of all Ex-U.S. companies in 2018, totaling $1.7 billion, one for a company in Phase III development and one in the market-stage.

FOLLOW-ON OFFERINGS FOR EX-U.S. R&D-STAGE COMPANIES BY DISEASE, 2009-2018

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	1	3	1	1	3	2	5	2	2	9
Neurology	0	0	1	0	2	0	3	3	0	3
Cardiovascular	0	0	2	1	1	1	0	1	2	2
Immunology	0	0	0	0	0	1	2	3	1	2
Metabolic	0	0	1	2	0	0	0	1	2	1
Infectious	0	0	0	0	0	0	1	2	2	1
Hematology	0	1	0	0	0	0	0	0	1	4
Other	0	0	0	0	0	0	2	1	0	3
Endocrine	0	0	0	1	1	0	0	1	1	1
Ophthalmology	0	0	0	0	0	0	0	0	1	2
Respiratory	0	0	0	0	0	1	1	0	0	0
Psychiatry	0	0	0	0	0	0	0	0	0	0
Gastrointestinal	0	0	0	0	0	0	0	0	0	0
Platform	0	0	0	0	0	0	0	0	0	0
Total (#)	1	4	5	5	7	5	14	14	12	28

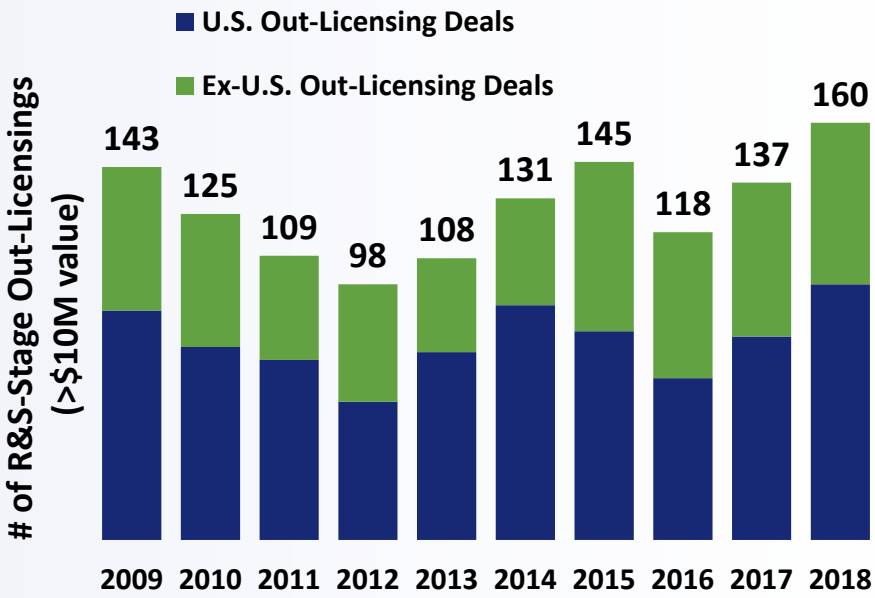
Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	$15	$91	$13	$18	$81	$109	$393	$195	$144	$1,278
Immunology	$0	$0	$0	$0	$0	$107	$662	$110	$266	$646
Hematology	$0	$81	$0	$0	$0	$0	$0	$0	$230	$519
Neurology	$0	$0	$32	$0	$130	$0	$239	$141	$0	$128
Endocrine	$0	$0	$0	$13	$45	$0	$0	$120	$155	$75
Other	$0	$0	$0	$0	$0	$0	$94	$75	$0	$211
Metabolic	$0	$0	$22	$65	$0	$0	$0	$119	$49	$70
Cardiovascular	$0	$0	$146	$37	$23	$24	$0	$12	$26	$41
Infectious	$0	$0	$0	$0	$0	$0	$39	$31	$90	$50
Ophthalmology	$0	$0	$0	$0	$0	$0	$0	$0	$16	$187
Respiratory	$0	$0	$0	$0	$0	$23	$98	$0	$0	$0
Psychiatry	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Gastrointestinal	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Platform	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Total ($M)	$15	$172	$212	$132	$279	$263	$1,525	$803	$976	$3,205

Figure 24. Follow-On Offerings for Ex-U.S. R&D-stage companies by diseases, 2009-2018. Amount raised ($M) and number of deals by disease. Disease categories are sorted by 10-year totals. Data includes novel drug and drug improvement R&D investment.

Out-Licensing

For licensing, we analyzed R&D-stage asset out-licensing activity from emerging companies for deals valued at more than $10 million to best represent deal flow and interest from large biopharmaceutical players. Globally, there was a 17% increase in the number of out-licensing deals from 137 in 2017 to 160 in 2018. The aggregate dollar amount paid upfront to emerging companies for out-licensed programs increased by 107% from $4.4 billion in 2017 to $9.1 billion in 2018. As seen in **Figure 26**, both the number of deals and the total upfront dollar amounts for 2018 are the highest amount seen over the 10-year period.

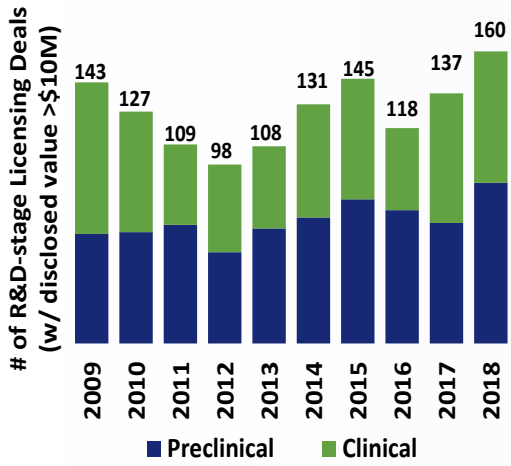
OUT-LICENSING OF R&D-STAGE THERAPEUTICS FROM EMERGING COMPANIES, 2009-2018

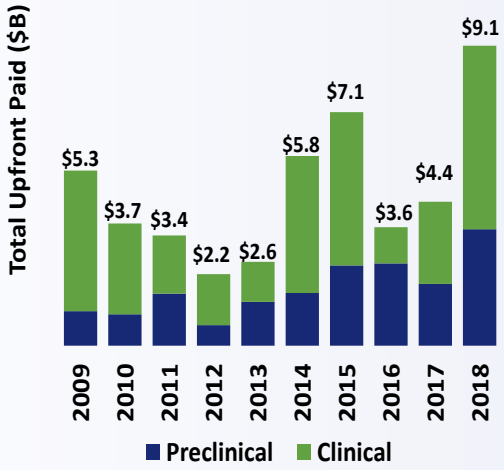


Region of Licensor	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
USA	88	74	69	53	72	90	80	62	78	98
Europe	34	37	30	32	26	34	41	40	39	35
ASIA	9	6	6	4	9	2	13	14	15	18
ROW	12	8	4	9	1	5	11	2	5	9
Total	143	125	109	98	108	131	145	118	137	160

Figure 25. Out-licensing for R&D-stage therapeutics from emerging companies by region, 2009-2018. Top: The number of licensing deals (with values above $10M) from U.S. versus Ex-U.S. emerging companies by year. Bottom: Total number of transactions per year by region.

OUT-LICENSING OF R&D-STAGE THERAPEUTICS FROM EMERGING COMPANIES, BY PHASE, 2009-2018





Number of Deals >$10M	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Preclinical	60	61	65	50	63	69	79	73	66	88
Phase I	15	10	10	13	14	16	16	9	21	17
Phase II	33	35	21	22	21	28	31	21	23	28
Phase III	35	21	13	13	10	18	19	15	27	27
Total	143	127	109	98	108	131	145	118	137	160

Upfront Amounts for Deals >$10M	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Preclinical	$1.1	$1.0	$1.6	$0.6	$1.3	$1.6	$2.4	$2.5	$1.9	$3.5
Phase I	$0.5	$0.1	$0.2	$0.2	$0.5	$0.5	$1.8	$0.0	$0.7	$0.4
Phase II	$1.5	$2.0	$0.6	$0.9	$0.5	$1.5	$1.8	$0.6	$1.2	$1.7
Phase III	$2.2	$0.6	$1.0	$0.5	$0.2	$2.2	$1.0	$0.5	$0.6	$3.5
Total	$5.3	$3.7	$3.4	$2.2	$2.6	$5.8	$7.1	$3.6	$4.4	$9.1

Total Potential Deal Amounts for Deals >$10M	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Preclinical	$10.9	$18.2	$14.1	$13.8	$15.2	$17.2	$29.7	$45.1	$34.1	$55.9
Phase I	$5.2	$2.5	$4.1	$2.8	$8.0	$3.5	$8.6	$1.5	$10.3	$6.0
Phase II	$8.7	$13.4	$6.4	$5.7	$4.4	$10.8	$13.0	$6.8	$5.7	$17.8
Phase III	$8.2	$4.1	$5.2	$3.4	$1.7	$9.6	$4.9	$3.0	$5.0	$11.6
Total	$33.0	$38.2	$29.8	$25.7	$29.3	$41.1	$56.2	$56.4	$55.1	$91.3

Figure 26. Out-licensing for global R&D-stage therapeutics, 2009-2018. Top: Total number of R&-stage out-licensing transactions and total upfront dollars per year for preclinical and clinical-stage assets. Bottom: Tables indicate the number of transactions, upfront total amounts (for deals greater than $10M), and total potential deal value (for deals greater than $10M), by year and by phase of development. Aggregate potential values include all regulatory and sales milestones.

The majority of the 160 licensing deals in 2018 were for preclinical-stage (88) assets, accounting for 55% of all transactions. This is the highest number of preclinical-stage transactions seen during the 10-year period. In 2018, the amount of upfront payments for preclinical-stage assets was equal to those for Phase III stage assets ($3.5B). However, the total potential value for pre-clinical stage assets far exceeded Phase III assets ($55.9 B vs. $11.6B). (Potential values include all regulatory and sales milestones agreed to in the licensing deal).

Oncology R&D-stage out-licensing deals maintained their dominance across all phases and all disease areas in 2018. The number of deals valued at above $10 million for oncology reached 57, the second highest year over the 10-year period, only slightly behind 2015 which had 58. Although this is slightly less than 2015 in terms of number of deals, the aggregate amount of upfront payments for oncology ($3.8 B) was the highest level of the decade.

As has been the case for the last nine years, neurology was the second most active disease area in terms of deal volume with 20 R&D-stage deals. Upfront payments in neurology came in at $2.1 billion, a staggering increase over the previous two years ($229 and $384 million for 2016 and 2017, respectively). The majority of this increase came from a single preclinical-stage deal with a company for multiple antisense therapies for a wide range of neurological conditions that received nearly a billion dollars upfront.

OUT-LICENSING OF R&D-STAGE THERAPEUTICS FROM EMERGING COMPANY BY DISEASE, 2009-2018

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	33	26	36	25	33	52	58	53	47	57
Neurology	22	21	9	14	17	11	18	11	12	20
Platform	14	14	10	12	11	5	9	11	9	7
Other	5	10	10	12	7	13	9	7	9	13
Infectious Disease	19	10	7	8	5	11	8	3	7	12
Immunology	12	10	13	6	8	6	6	6	11	6
Endocrine	8	16	5	1	5	7	12	3	9	11
Metabolic	6	4	3	4	5	3	4	6	7	11
Cardiovascular	5	4	6	2	7	4	4	3	5	7
Hematology	4	2	2	4	5	4	5	2	4	2
Ophthalmology	2	3	2	2	1	4	6	4	7	3
Gastrointestinal	7	0	1	2	1	6	1	4	4	6
Respiratory	3	4	2	4	2	4	4	2	3	2
Psychiatry	3	3	3	2	1	1	1	3	3	3
Total (#)	143	127	109	98	108	131	145	118	137	160

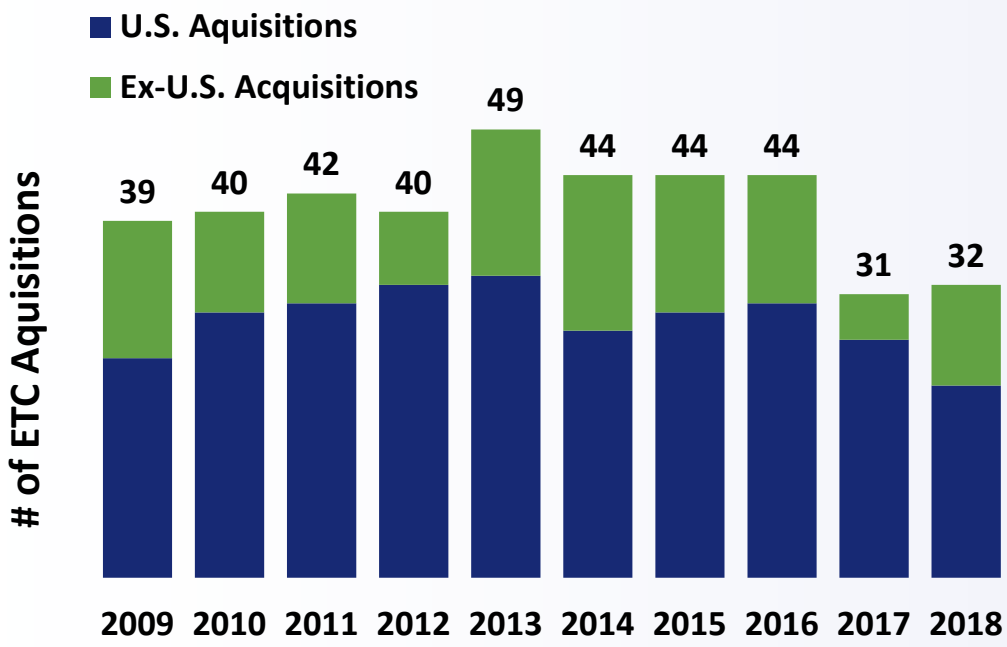
Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	$919	$533	$1,139	$804	$874	$1,697	$3,421	$1,981	$2,256	$3,780
Neurology	$1,589	$264	$128	$231	$296	$586	$327	$229	$384	$2,115
Immunology	$396	$189	$259	$163	$261	$82	$898	$259	$311	$104
Other	$107	$681	$106	$310	$95	$152	$462	$195	$113	$526
Endocrine	$113	$476	$588	$8	$96	$530	$377	$92	$147	$309
Cardiovascular	$175	$737	$72	$6	$120	$91	$82	$75	$227	$1,085
Platform	$139	$230	$487	$71	$396	$142	$377	$234	$139	$68
Infectious Disease	$797	$304	$197	$257	$58	$196	$65	$6	$24	$366
Metabolic	$185	$166	$33	$95	$62	$738	$230	$120	$69	$399
Gastrointestinal	$266	$0	$50	$20	$70	$798	$0	$185	$116	$170
Ophthalmology	$36	$25	$60	$163	$10	$418	$248	$51	$161	$78
Respiratory	$275	$52	$9	$1	$50	$57	$380	$40	$234	$17
Hematology	$102	$30	$25	$38	$66	$260	$230	$125	$133	$5
Psychiatry	$231	$32	$202	$11	$98	$25	$10	$13	$67	$105
Total ($M)	$5,330	$3,719	$3,355	$2,177	$2,553	$5,772	$7,105	$3,604	$4,381	$9,126

Figure 27. Number of out-licensing deals by disease and aggregate amount paid upfront ($M) in deals of R&D-stage assets from global emerging companies, 2009-2018, for deals with disclosed potential value above $10M. Disease categories are sorted by 10-year totals. Data includes novel drug and drug improvement R&D investment.

Acquisitions

The number of global acquisitions for both R&D-stage and market-stage emerging companies showed a slight increase in 2018 with 32 transactions, below the decade average of 41, but just above the 31 seen in 2017. For the U.S., 2018 marks the lowest year for acquisitions over the last decade, with only 21 transactions. However, in dollar terms, total potential acquisition value for U.S. companies hit a record $26.4 billion (including $2 billion from market-stage companies). Europe saw 9 emerging company acquisitions (28%) in 2018, more than doubling the four acquisitions in 2017. Both Asia and the ROW category each had 1 acquisition in 2018, from Australia and Canada respectively.

EMERGING COMPANY ACQUISITIONS WORLDWIDE, 2009-2018



Acquistion Target Region	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
USA	24	29	30	32	33	27	29	30	26	21
Europe	9	9	9	6	9	12	12	8	4	9
ASIA	2	1	1	1	1	1	2	0	1	1
ROW	4	1	2	1	6	4	1	6	0	1
Total	39	40	42	40	49	44	44	44	31	32

Figure 28. Top: Number of acquisitions for global emerging therapeutic companies in both R&D-stage and Market-stage (with buyout values above $10M), by phase, 2009-2018. Bottom: Number of acquisitions for global emerging therapeutic companies in both R&D-stage and Market-stage (with buyout values over $10M), by region, 2009-2018.

For this section on acquisitions, we report on R&D-stage emerging company acquisitions first, followed by Market-stage emerging company acquisitions.

The number of acquisitions of R&D-stage emerging therapeutic companies rebounded to 28 from the decade low of 21 in 2017 (**Figure 29a**). This is very close to the decade average of 29 acquisitions per year. The total upfront amount paid for these 28 R&D-stage companies was $32.5 billion. This is a record amount and nearly double the $17.6 billion in 2017. The majority of this increase was for Phase II and III stage company acquisitions (**Figure 29a**). The median price paid for a R&D-stage emerging company in 2017 was $137 million in upfront payments and $425 million when all contingent value right payments are included. For a number of emerging company acquisitions, the full acquisition price may only be realized on execution of key regulatory events, for example an eventual FDA approval of a Phase III asset.

U.S.-based emerging therapeutic companies accounted for 66% of global acquisitions in 2018, followed by Europe (28%), ROW (7%, primarily from Israel and Canada) and Asia (3%, primarily from Australia).[1]

In 2018, there were three R&D-stage emerging company acquisitions above $5 billion in total value: Juno was acquired by Celgene for $9 billion, AveXis was acquired by Novartis for $8.7 billion (neuromuscular gene therapy), and Ablynx NV was acquired by Sanofi for $5.1 billion. The acquisition of Kite by Gilead for $11.9 billion in 2017 was an outlier, making up 67% of the year's $17.6 billion in purchases.

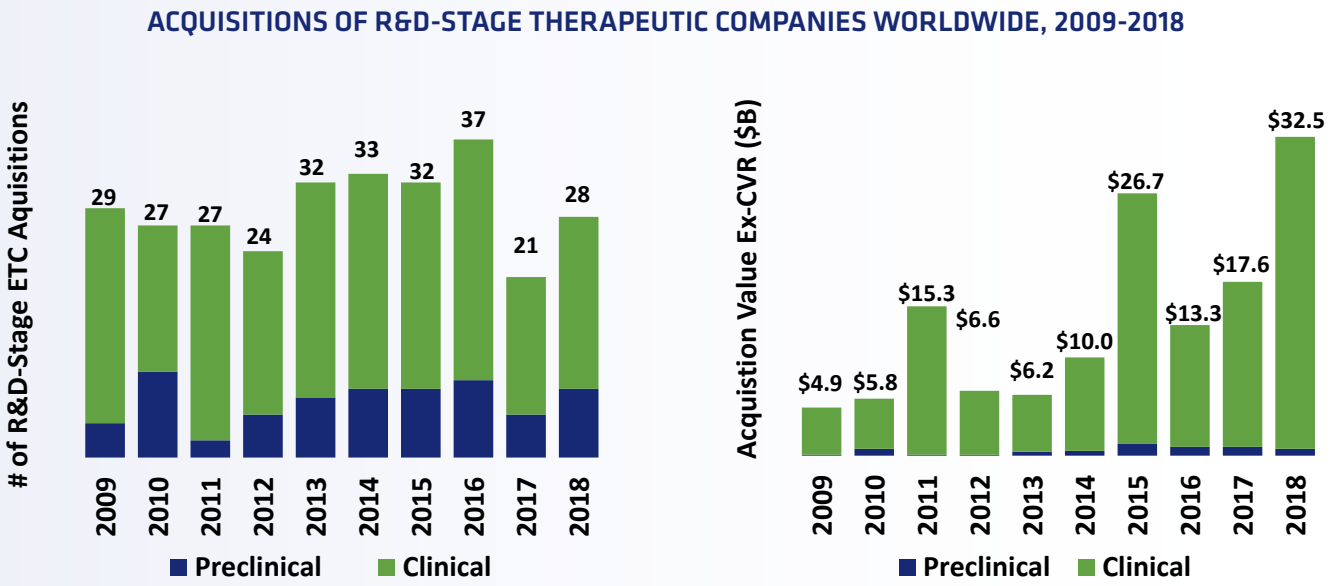


Figure 29a. Left: Number of acquisitions of global R&D-stage emerging therapeutic companies, 2009-2018. Right: Total dollars spent upfront on global acquisitions of R&D-stage emerging therapeutic companies, 2009-2018.

[1] See Methodology for regional definitions. Asia as defined for this report includes the entire Asia Pacific region.

Only 4 Market-stage emerging therapeutic companies (those with sales below $1) were acquired in 2018, the lowest in a decade (**Figure 29b**). Additionally, 2018 had the lowest amount of total upfront dollars paid for market-stage emerging therapeutic companies ($2.2 billion) in a decade.

It should be noted that the largest acquisitions over the last few years have been of companies with more than $1 billion in sales (data not shown). For example, 2018's acquisitions of Shire by Takeda ($60 billion) and Bioverativ by Sanofi ($11.6 billion). In 2017, Actelion was acquired by Johnson & Johnson for $30 billion and in 2019 Eli Lily acquired Celgene for $74 billion (the highest amount paid for an acquisition in a decade). These M&A deals are larger than 99% of all emerging company acquisitions.

Taken together, it appears larger biopharmaceutical companies are now targeting large commercial-stage biotechnology companies or companies with new innovative medicines in pivotal trials or under FDA review for marketing approval.

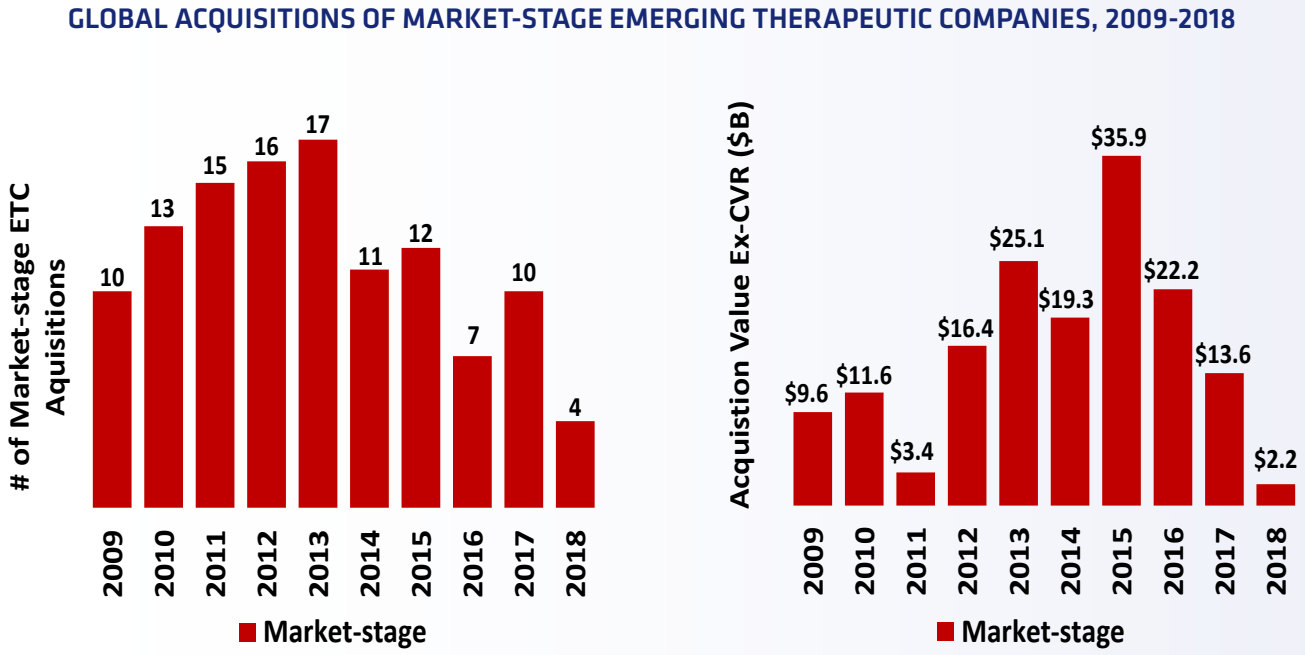


Figure 29b. Left: Number of global acquisitions of market-stage emerging therapeutic companies (companies with <$1B sales), 2009-2018. Right: Total dollars spent upfront on global acquisitions of market-stage emerging therapeutic companies (companies with <$1B sales), 2009-2018.

GLOBAL EMERGING COMPANY ACQUISITIONS, BY PHASE, 2009-2018

Number of Acquisitions >$10M	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Preclinical	4	10	2	5	7	8	8	9	5	8
Phase I	3	2	5	3	2	6	8	4	3	3
Phase II	15	7	14	12	16	10	9	15	8	10
Phase III	7	8	6	4	7	9	7	9	5	7
Marketed	10	13	15	16	17	11	12	7	10	4
Total	39	40	42	40	49	44	44	44	31	32

Upfront Amounts for Acquisitions >$10M	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Preclinical	$0.1	$0.7	$0.1	$0.1	$0.4	$0.5	$1.2	$0.9	$0.9	$0.7
Phase I	$0.1	$0.4	$0.4	$0.4	$1.0	$1.0	$0.7	$0.3	$0.8	$0.4
Phase II	$2.7	$1.3	$13.3	$4.4	$2.5	$2.6	$2.4	$9.3	$2.8	$13.3
Phase III	$2.0	$3.4	$1.4	$1.6	$2.3	$5.9	$22.4	$2.7	$13.2	$18.0
Marketed	$9.6	$11.6	$3.4	$16.4	$25.1	$19.3	$35.9	$22.2	$13.6	$2.2
Total	$15	$17	$19	$23	$31	$29	$63	$35	$31	$35

Total Potential Amounts for Acquisitions >$10M	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Preclinical	$0.1	$0.8	$0.5	$0.3	$1.2	$1.6	$2.1	$1.5	$4.2	$1.3
Phase I	$0.1	$1.2	$0.4	$1.5	$1.4	$2.3	$2.3	$1.4	$1.8	$2.6
Phase II	$4.5	$1.4	$14.8	$5.5	$4.1	$3.6	$7.8	$18.2	$3.7	$14.8
Phase III	$2.9	$5.0	$2.2	$4.2	$3.3	$7.0	$23.1	$3.0	$13.2	$24.0
Marketed	$10.2	$11.6	$4.1	$17.1	$25.4	$20.5	$37.0	$22.2	$13.9	$2.4
Total	$18	$20	$22	$29	$35	$35	$72	$46	$37	$45

Figure 30. Top: Number of acquisitions for global emerging therapeutic companies (with buyout values above $10M), by phase, 2009-2018. Center: Acquisition upfront amounts for global emerging therapeutic companies, by phase. Bottom: Total dollars (upfront plus milestones contingent value rights) global emerging therapeutic companies.

There were notable changes in acquisition activity by disease area in 2018 vs. 2017. The number of oncology acquisitions (valued at >$10 million USD) rebounded to the highest of all 12 areas we group indications in 2018. Neurology also rebounded from one to four acquisitions. Decreases were seen in metabolic, endocrine, immunology, and hematology in 2018. For all areas outside oncology and neurology, only a few acquisitions occurred in 2018, some without a single acquisition with disclosed values above $10 million (**Figure 31**).

GLOBAL AQUISITIONS OF R&D-STAGE THERAPEUTIC COMPANIES BY DISEASE, 2009-2018

Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	8	4	11	7	10	12	5	13	4	10
Neurology	4	2	3	3	1	5	4	5	1	4
Infectious Disease	6	0	2	3	7	4	1	1	1	2
Platform	1	8	1	3	2	3	5	2	0	2
Endocrine	0	3	1	1	3	3	2	2	2	0
Metabolic	0	1	1	1	3	1	3	0	4	3
Immunology	2	1	2	1	0	1	2	2	3	2
Other	2	1	3	1	0	0	1	5	1	1
Cardiovascular	2	1	1	1	2	1	2	0	1	1
Respiratory	0	3	1	2	2	0	2	2	0	0
Ophthalmology	3	0	0	0	1	2	2	3	0	1
Hematology	1	0	0	1	1	0	0	1	3	1
Gastrointestinal	0	2	1	0	0	1	1	0	0	1
Psychiatry	0	1	0	0	0	0	2	0	1	0
Total (#)	29	27	27	24	32	33	32	36	21	28

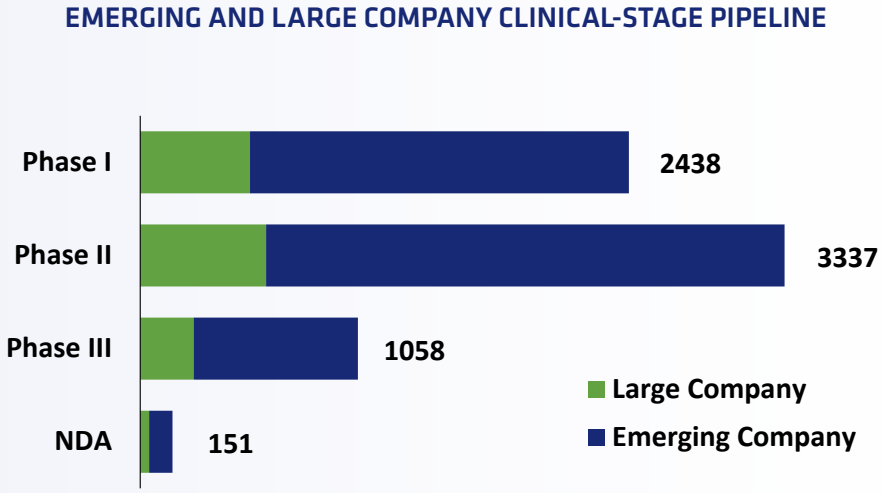
Disease Area	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Oncology	$1,773	$2,833	$2,218	$2,175	$2,616	$1,435	$1,011	$8,931	$13,922	$15,274
Infectious Disease	$1,187	$0	$11,412	$2,131	$1,339	$5,827	$190	$0	$13	$458
Metabolic	$0	$22	$610	$293	$74	$89	$8,716	$0	$536	$9,589
Gastrointestinal	$0	$390	$21	$0	$0	$1,027	$7,332	$0	$0	$621
Neurology	$703	$695	$210	$46	$37	$952	$3,644	$1,322	$1,027	$340
Hematology	$255	$0	$0	$94	$240	$0	$0	$665	$571	$5,123
Endocrine	$0	$472	$71	$315	$730	$107	$2,722	$594	$180	$0
Immunology	$221	$102	$186	$1,272	$0	$260	$330	$275	$620	$477
Other	$302	$70	$175	$9	$0	$0	$229	$815	$534	$195
Respiratory	$0	$204	$328	$178	$600	$0	$260	$500	$0	$0
Platform	$29	$598	$10	$111	$51	$175	$541	$50	$0	$133
Cardiovascular	$153	$165	$10	$3	$336	$42	$600	$0	$137	$141
Ophthalmology	$298	$0	$0	$0	$160	$67	$679	$170	$0	$109
Psychiatry	$0	$226	$0	$0	$0	$0	$462	$0	$100	$0
Total ($M)	$4,921	$5,777	$15,251	$6,627	$6,183	$9,981	$26,716	$13,322	$17,640	$32,460

Figure 31. R&D-stage acquisitions, 2009-2018. Aggregated numbers of full company acquisitions (top) and the total value of non-conditional (ex-CVR) acquisition cost (below), by year, for acquisitions with disclosed potential value above $10M. Disease categories are sorted by 10-year totals. Data includes novel drug and drug improvement R&D investment.

Clinical Pipeline

The current global industry pipeline contains 6,984 clinical-stage drug programs (**Figure 32**). Emerging companies account for 5,067 (73%) of these drug indication programs under development, either independently or partnered. This is an increase of 304 programs from emerging companies, up from 4,763 in March 2018. Almost no increase in the total number of programs was found for large companies (1,917 in 2019 vs. 1,916 in 2018).

The influence of emerging companies on upcoming FDA approvals is illustrated by the fact that 94 of the 151 submitted NDA/BLAs (62%) involve an emerging company **(Figure 32**).



Pipeline	Phase I	Phase II	Phase III	NDA	Total
Emerging Company	1731	2527	715	94	5067
Large Company	707	810	343	57	1917
Total Industry Pipeline	2438	3337	1058	151	6984
% of Total Pipeline	35%	48%	15%	2%	100%

Figure 32. Number of clinical Drug/Indication programs (Phase I, II, III, and NDA/BLA-stage) in the pipeline at emerging therapeutic companies and large biopharmaceutical developers. Based on analysis of the BioMedTracker database accessed April 2019. BioMedTracker programs shown are of global origin, but with intentions to eventually file for regulatory approval in the U.S.

Roughly 45% of emerging company programs are now partnered with other companies, demonstrating the importance of licensing collaborations in the biopharmaceutical industry. The degree of partnered programs varies by phase. For Phase III emerging therapeutic company programs, 53% are partnered. Phase II and Phase I emerging therapeutic company programs are 46% and 38% partnered, respectively.

The global clinical pipeline was broken out into 13 major disease areas (**Figure 32**). Oncology accounts for the largest percentage of the clinical pipeline (41%), followed by neurology (11%) which includes pain, and infectious disease (8%) and immunology (8%).

The partnered and unpartnered programs, by disease area, can be found in **Figure 32**. Although each disease area contains more unpartnered than partnered programs, no disease area is below 35% partnered. For example, 36% of emerging company programs in cardiovascular and infectious disease are partnered. Oncology has the highest percentage of partnered programs (50%).

GLOBAL INDUSTRY CLINICAL PIPELINE BY REGION

Total Pipeline:

Region	P1	P2	P3	NDA/ BLA	TOTAL	% of Total
U.S.	1408	1853	508	86	3855	55%
Europe	630	964	365	31	1990	28%
Asia	329	352	128	25	834	12%
ROW	71	168	57	9	305	4%
Global	2438	3337	1058	151	6984	100%

Emerging Company Pipeline:

Region	P1	P2	P3	NDA/ BLA	TOTAL	% of Total
U.S.	1096	1547	391	59	3093	44%
Europe	351	584	208	16	1159	17%
Asia	219	237	70	11	537	8%
ROW	65	159	46	8	278	4%
Global	1731	2527	715	94	5067	73%

Figure 33. Number of global emerging and large therapeutic companies' clinical programs for by disease area and phase, as of April 2019.

GLOBAL INDUSTRY CLINICAL PIPELINE BY DISEASE AREA

Disease	P1	P2	P3	NDA/BLA	Total	% of Total
Oncology	1196	1386	274	24	2880	41%
Neurology	263	335	142	24	764	11%
Infectious Disease	208	224	79	15	526	8%
Immunology	156	248	102	20	526	8%
Other	125	252	105	13	495	7%
Endocrine	113	168	60	13	354	5%
Cardiovascular	67	112	56	6	241	3%
Ophthalmology	35	146	57	6	244	3%
Respiratory	74	122	31	1	228	3%
Metabolic	61	105	44	9	219	3%
Gastroinstential	58	113	33	7	211	3%
Hematology	35	61	42	9	147	2%
Psychiatry	47	65	33	4	149	2%
Total	2438	3337	1058	151	6984	100%

Figure 34. Number of global emerging and large therapeutic companies' clinical programs, by disease area and phase, as of April 2019.

EMERGING THERAPEUTIC COMPANY (ETC) CLINICAL PIPELINE – PARTNERED VS UNPARTNERED

Disease	Type	P1	P2	P3	NDA/BLA	Total
Oncology	ETC Unpartnered	465	474	70	1	1010
	ETC Partnered	354	531	110	7	1002
Neurology	ETC Unpartnered	151	166	53	6	376
	ETC Partnered	66	112	51	9	238
Infectious Disease	ETC Unpartnered	115	105	26	6	252
	ETC Partnered	43	66	28	4	141
Immunology	ETC Unpartnered	55	102	27	3	187
	ETC Partnered	42	72	29	4	147
Other	ETC Unpartnered	51	119	33	7	210
	ETC Partnered	27	85	44	4	160
Endocrine	ETC Unpartnered	60	75	21	2	158
	ETC Partnered	18	63	19	8	108
Cardiovascular	ETC Unpartnered	37	65	25	1	128
	ETC Partnered	14	31	22	4	71
Ophthalmology	ETC Unpartnered	19	73	24	3	119
	ETC Partnered	9	47	19	2	77
Respiratory	ETC Unpartnered	33	39	5	0	77
	ETC Partnered	19	41	8	1	69
Metabolic	ETC Unpartnered	21	46	18	4	89
	ETC Partnered	20	38	19	2	79
Gastroinstential	ETC Unpartnered	27	48	9	0	84
	ETC Partnered	18	37	9	4	68
Hematology	ETC Unpartnered	22	20	15	2	59
	ETC Partnered	10	26	13	6	55
Psychiatry	ETC Unpartnered	22	27	11	2	62
	ETC Partnered	13	19	7	2	41
	Total ETC Unpartnered	1078	1359	337	37	2811
	Total ETC Partnered	653	1168	378	57	2256
	Total Large Companies	707	810	343	57	1917
	Total	2438	3337	1058	151	6984

Figure 35. Number of clinical programs by disease area for emerging therapeutic companies, partnered vs. unpartnered, as of April 2019.

Rare Disease

According to Global Genes there are 7,000 rare diseases that cumulatively affect 30 million Americans.[2] Here we report on investment and deal-making for global emerging companies working to bring new medicines to these patients, with an emphasis on diseases outside oncology. Many oncology companies have multiple cancer programs (such as rare and non-rare sub-indications) at similar stages of development. This makes categorization by lead indication less precise. For the pipeline of Orphan designated drugs, we report both cancer and non-cancer programs by phase.

Venture Capital: Over the last ten years, there has been an increase in global investment into rare diseases (ex-oncology), with the highest amount seen in 2018 ($2 billion), (**Figure 36**).

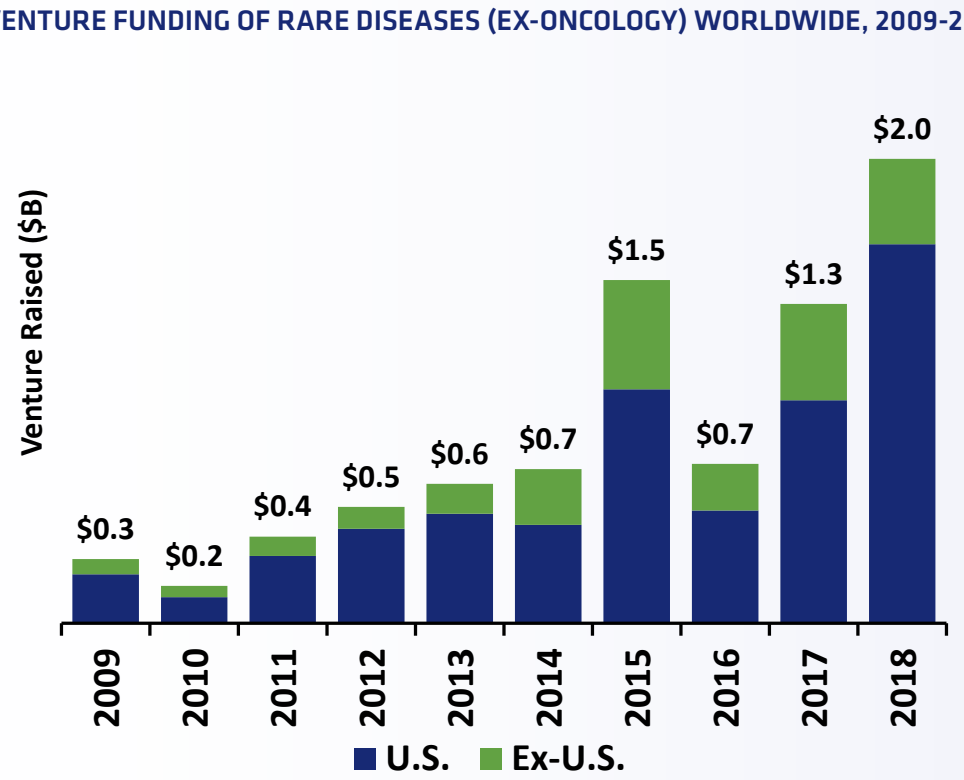


Figure 36. Global venture funding ($M) into emerging therapeutic companies with a lead drug in a rare disease (ex-oncology), 2009-2018.

IPOs: The number of rare disease IPOs (ex-oncology) was up from just 10 in 2017 to 14 in 2018. The total amount raised in 2018 was $1.4 billion.

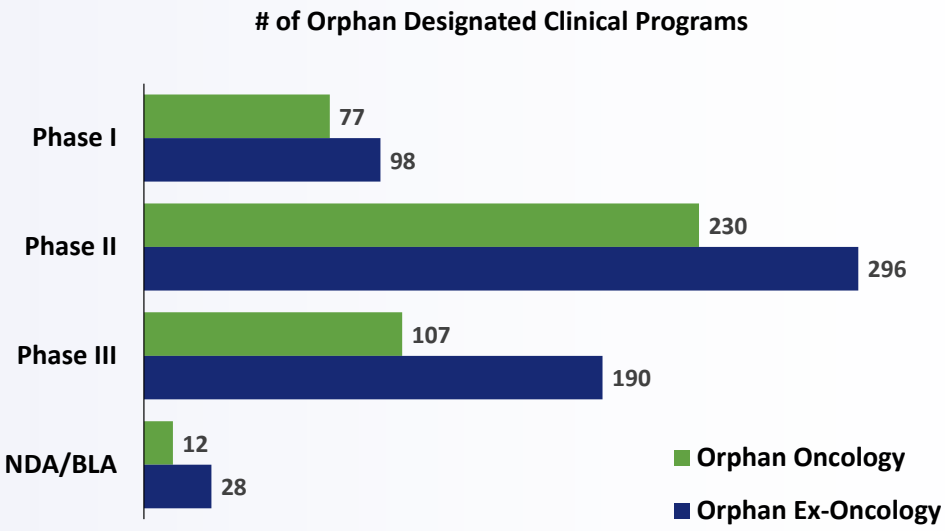
Licensing: The number of global licensing transactions (>$10M potential value) for rare disease drugs (ex-oncology) has grown from 6 in 2009 to 30 in 2018. Total upfront payments from these deals has grown from $0.3 billion in 2009 to $2 billion in 2018.

Acquisitions: The number of acquisitions of rare disease emerging companies (ex-oncology) has been increasing throughout the decade from 5 in 2009 to 11 in 2018. The total amount spent on these acquisitions has grown from $1 billion in 2009 to $26.7 billion in 2018.

[2] http://globalgenes.org

Rare Disease Pipeline: Including rare cancers, the number of Orphan drug programs has increased from 806 in 2017, to 964 in 2018, to 1038 as of April 2019. Small emerging companies account for 85% of all Orphan-designated products in clinical development (**Figure 37**). As of April 2019, there were 612 ex-oncology rare disease programs and 426 rare cancer programs.

ORPHAN DRUG PIPELINE FOR GLOBAL EMERGING THERAPEUTIC COMPANIES



Orphan Disease Area	Phase I	Phase II	Phase III	NDA/BLA	Total
Orphan Oncology	77	230	107	12	426
Orphan Ex-Oncology	98	296	190	28	612
Total Orphan Programs	175	526	297	40	1038

Orphan Ex-Oncology	Phase I	Phase II	Phase III	NDA/BLA	Total
Emerging Co. Programs	87	257	159	21	524
Large Co. Programs	11	39	31	7	88
Total Orphan Ex-Oncology	98	296	190	28	612

Figure 37: Clinical pipeline for all Orphan Designated products (including rare cancers) developed by global emerging companies and large companies as of April 2019. Large multinational companies developing licensed drugs from a partnership with an emerging company is counted under emerging companies.

Discussion

The aim of this annual study is to accurately define the levels of funding and deal interest in emerging therapeutic companies by disease area and stage of development. Tracking this activity over a 10-year time period allows for the identification of strengths and weaknesses across this often-fragile ecosystem of drug innovation.

In this 5th annual report, covering 2009-2018, decade highs were reached in 2018 for both investments and deal-making. However, these increases continue to be concentrated in oncology and rare diseases, not in highly prevalent chronic diseases areas. This points to a bifurcated industry where it remains difficult to find funding in some indications, and record levels reached in others. To investigate this developing trend, BIO has published a series of reports (available at www.bio.org/iareports) that focuses on individual chronic indications and the current state of innovation.

With this concerning trend aside, there are five key takeaways from 2018: 1) U.S. start-ups receiving first-time Series A funding finally broke through the previous ceiling in place for decades, with 109 financings; 2) Venture investment into innovative U.S. therapeutic companies continues to outpace Europe (5.7x), Asia (4.6x), and the rest of the world (35x); 3) Chinese companies set an historical precedent with the highest percentage increase (600%) in Ex-U.S. venture funding over the last decade; 4) Public market financing is healthy, as exemplified by recent IPOs and follow-on activity; and 5) Funding via licensing remains strong overall, especially for rare disease assets.

Investment interest in biotechnology has strengthened in part due to increased productivity as measured by FDA drug approvals (reaching a record high with 59 novel drug approvals in 2018), but also due to key policy changes over this last decade. The 2012 Prescription Drug User Fee Act (PUDFA V) agreement put in place the now widely recognized Breakthrough Therapy Designation, and more recently, the 21st Century Cures Act (2016) and PDUFA VI agreement (2017) have been positive for innovation in the industry. Additionally, the 2012 Jumpstart Our Business Startups (JOBS) Act provided pre-revenue companies with more efficient access to public markets.

Emerging company innovation, on the heels of these policy changes, now drives 73% of the clinical-stage pipeline. It is imperative that the right regulatory and financial policy environment be maintained for this group of companies to transform the future of medicine. These small companies depend on strong intellectual property protections, regulatory benefit-risk balance, financial incentives for R&D and investment, and a reimbursement environment that appropriately values and rewards such high-risk investment for medical innovation.

Methodology

Emerging Therapeutic Company definition: All companies analyzed for this report are "Emerging Therapeutic" companies that are a) developing therapeutics with a lead drug in R&D, or b) have a drug on the market, but have less than $1 billion in sales at the time of the transaction.

Novel vs. Improvement R&D: We grouped companies into two categories for level of innovation: novel R&D pursuing a new chemical entity, and R&D that expands the properties, availability, patient experience, etc. of an already-approved chemical entity. In the first category, novel R&D, we included in-licensed assets with prior data, such as spin-outs from big pharmaceutical companies. The lead drug for the novel category cannot have had a prior approval for any indication. The second category, drug improvement, included delivery technologies such as nanotechnology, lipids (micelles), new adjuvants for approved vaccines, extended release and prolonged half-life chemical modifications (conjugates and linkers, including pegylated variants), patches, topical creams, implanted delivery devices, needle-less injections, as well as reformulation of an approved drug, repurposing of an approved drug, and nutraceuticals.

Company Category: Each event (Venture, IPO, FOPO, Licensing, or Acquisitions) was tagged by the company's lead program disease area and phase of development as of the date of payment for Venture, traction for IPO/FOPO, or announcement of deal for Licensing and Acquisitions.

Disease Categorizing: Vaccines include both bacterial and viral vaccines. Thus, all other infectious disease categories are for small molecule or large molecule approaches ex-vaccine. Oncology vaccines are tagged as vaccines if a true antigen (often peptides) is being utilized and will have the modality tagged with vaccine instead of large molecule. Thus, oncology vaccines do not show up under vaccines within infectious disease. This allows us to sort vaccines across all disease areas. "Other" in Infectious Disease refers mainly to anti-parasitic medicines and head lice treatments.

Wound healing was placed under dermatology if directly related to skin injury, but if directly affecting the immune system it is labeled under immunology. Immunology is ex-GI diseases. This is significant as some databases will place IBD under inflammation, but we chose to place it under gastrointestinal.

Platform refers to molecular platforms only, not target- or hypothesis-driven platforms. For example, a company focused on the mTOR pathway would not be a platform company, but a company designing bispecific Fab fragments would count as platform.

Strokes involving the brain are classified under neurology, but if designed for heart stroke in patients they are labeled as cardiovascular.

Osteoporosis falls under endocrine, and Osteoarthritis was placed under "Other." Also under "Other" are dermatology, allergy, musculoskeletal diseases, otology (ear diseases), periodontitis, urology/genitourinary, non-viral liver diseases, fertility drugs, and treatments for side effects of chemotherapy or radiation.

Venture Capital: For U.S. venture capital, the primary data source used was the Cortellis Competitive Intelligence database from Clarivate Analytics & Thomson Reuters. This was supplemented with three others: EvaluatePharma, Informa's Strategic Transactions, and BioCentury's BCIQ database. Ex-U.S. venture capital was sourced primarily from EvaluatePharma and BioCentury's BCIQ database. Further investigation of company R&D and financings was complemented with Factset and SEC filings as well as Fierce Biotech, Xconomy, BiotechGate, and company press releases. Equity investments from 2009 to 2018 were aggregated, and duplicates and non-drug company financing events were removed. Generics, distribution, and pharmacy companies were also excluded. Cases where private money was raised for the sole purpose of acquiring an existing company were also excluded. Equity investments in this study are predominantly venture in nature, with some differences at the Seed stage where angel investors, family offices, and other non-venture capital investors have an impact. Additionally, debt financing, bridge loans, government grants, and disease/patient foundation grants were also excluded.

As mentioned above, the tagging is based on the date of actual funding, not commitment to future tranches. For example, large Series A rounds can be spread out into payments stretching beyond a single year when press releases and major media outlets report a financing event. Each year of funding, for each round, investment was labeled by one of 14 major categories (13 diseases plus platform technologies).

Series financings often occur over multiple years as tranche payments. For example, a Series A round can have the sequence of A1, A2, A3 rounds within the same year or in different years. These were accounted for by year such that the accounting is for companies financed per year, not payments/tranches per year. For example, a company with A1, A2, and A3 payments in 2012 would be treated as a single company financing in 2012, not three separate Series A round financings. If the A1, A2, and A3 rounds occurred in 2011, 2012, and 2013, then these would be counted as one Series A round investment per year. This enables an accurate accounting of breadth of funding on a yearly basis.

IPOs: BIO Industry Analysis uses IPO amounts reported on the Nasdaq.com website, S-1 filings with the SEC. IPOs are tracked from a variety of news feeds including EndPoints, Biocentury, BioWorld, FierceBiotech. Disease areas and phase were tagged according to lead product in R&D at the time of investment.

Follow-on offerings: Biocentury was the primary data source for follow-on offerings. Only new shares issued in a follow-on offering valued at more than $10 million were included. Values exclude sales of shares by inside investors. Disease areas and phase were tagged according to lead product in R&D at the time of investment.

Licensing: Informa's Strategic Transactions database and the Cortellis Deals Intelligence database from Clarivate and Thomson Reuters (formerly Recap) were the primary data sources for licensing. Disease areas and phase were tagged according to lead product in R&D at the time of the deal.

Pipeline: BioMedTracker was the primary source for pipeline data. We analyzed each company and partner for inclusion as an emerging company or large biopharmaceutical company, defined by below or above $1 billion in sales, respectively.

Acquisitions: The primary data source for acquisitions was the Informa Strategic Transactions database. This was supplemented with the Cortellis Deals Intelligence database from Clarivate and Thomson Reuters (formerly Recap) and EvaluatePharma. Disease areas and phase were tagged according to lead product in R&D at the time of the deal. For global acquisition data, we only reported upfront payments to more accurately reflect the actual money flow into small company investors. Although Contingent Value Rights (CVRs) structures are now being used extensively in emerging company acquisitions (66% of acquisitions in our dataset), the upfront dollars are an immediate, guaranteed commitment from the partner or acquirer. The data presented for acquisitions includes both R&D-stage emerging companies (with a lead product in Preclinical, Phase I, Phase II, or Phase III testing), and market-stage emerging companies (with an approved product but with under $1 billion in product sales). By focusing only on emerging companies, this data may differ from other currently available reports that often include large company acquisitions.

Rare Disease: Although many oncology companies do seek Orphan Drug status for rare cancer indications, we only found a few unique cases where a company's lead program was for a specific rare cancer. Most oncology companies analyzed had multiple lead cancer areas and indications often switched from lead to non-lead status from year to year. Thus we focused the rare disease section on ex-oncology rare diseases. The pipeline section for Orphan designated drug programs reports data on both oncology and ex-oncology rare disease programs.

Countries: For Europe the following countries were included: Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Italy, Ireland, Malta, Netherlands, Norway, Poland, Spain, Sweden, Switzerland, United Kingdom. For Asia, the Pacific region is included: Australia, China, India, Hong Kong, Japan, Malaysia, New Zealand, Singapore, South Korea, Taiwan. For ROW: Bermuda, Canada, Cayman Islands, Chile, Israel, Russia.

Appendix

VENTURE FUNDING OF GLOBAL THERAPEUTIC COMPANIES BY DISEASE, 2009-2018

US Investment ($M) 2009-2018	U.S. Venture		Ex-U.S. Venture		Total	
Oncology	$13.1	29%	$9.1	35%	$22.2	31%
Other	$3.4	7%	$4.3	16%	$7.6	11%
Neurology	$5.1	11%	$1.5	6%	$6.6	9%
Infectious	$5.0	11%	$1.6	6%	$6.5	9%
Platform	$4.2	9%	$2.1	8%	$6.3	9%
Endocrine	$3.4	7%	$1.3	5%	$4.7	6%
Immunology	$2.0	4%	$2.4	9%	$4.4	6%
Metabolic	$2.4	5%	$0.5	2%	$3.0	4%
Cardiovascular	$1.7	4%	$1.0	4%	$2.8	4%
Ophthalmology	$1.9	4%	$0.6	2%	$2.5	4%
Respiratory	$1.2	3%	$0.4	2%	$1.7	2%
Gastroinstestinal	$0.7	2%	$0.7	3%	$1.5	2%
Hematology	$1.0	2%	$0.4	2%	$1.4	2%
Psychiatry	$0.6	1%	$0.2	1%	$0.8	1%
Total	**$46**	**100%**	**$26**	**100%**	**$72**	**100%**

Figure A1. Ten-year total venture funding, by disease.

IPOS FOR GLOBAL EMERGING THERAPEUTIC COMPANIES, BY DISEASE, 2009-2018

US Investment ($M) 2009-2018	U.S. IPOs		Ex-U.S. IPOs		Total	
Oncology	$5.9	29%	$3.4	38%	$9.2	32%
Other	$1.9	9%	$1.1	13%	$3.0	11%
Neurology	$2.2	11%	$0.8	9%	$3.0	10%
Infectious	$1.5	8%	$0.8	9%	$2.3	8%
Metabolic	$1.9	10%	$0.4	4%	$2.3	8%
Cardiovascular	$1.6	8%	$0.4	4%	$2.0	7%
Ophthalmology	$1.2	6%	$0.4	5%	$1.6	6%
Endocrine	$1.0	5%	$0.6	6%	$1.6	5%
Inflammation	$0.7	3%	$0.5	6%	$1.3	4%
Hematology	$0.8	4%	$0.0	1%	$0.8	3%
Platform	$0.4	2%	$0.2	2%	$0.6	2%
Gastroinstestinal	$0.4	2%	$0.1	1%	$0.5	2%
Respiratory	$0.3	2%	$0.1	1%	$0.4	1%
Psychiatry	$0.3	2%	$0.0	0%	$0.3	1%
Total	**$20.2**	**100%**	**$8.7**	**100%**	**$28.9**	**100%**

Figure A2. Ten-year totals, by disease, for initial public offerings (IPOs) from emerging companies.

FOLLOW-ON OFFERINGS FOR GLOBAL EMERGING COMPANIES, BY DISEASE, 2009-2018

US Investment ($B) 2009-2018	U.S. Follow-Ons		Ex-U.S. Follow-Ons		Total	
Oncology	$23.9	28%	$3.7	26%	$27.7	28%
Neurology	$9.2	11%	$2.4	17%	$11.7	12%
Metabolic	$10.8	13%	$0.5	3%	$11.2	11%
Infectious	$10.1	12%	$0.8	5%	$10.9	11%
Hematology	$5.9	7%	$0.9	7%	$6.9	7%
Other	$5.4	6%	$0.9	7%	$6.3	6%
Immunology	$4.0	5%	$2.1	14%	$6.0	6%
Endocrine	$4.7	6%	$0.5	3%	$5.2	5%
Cardiovascular	$3.5	4%	$1.3	9%	$4.8	5%
Gastroinstestinal	$2.5	3%	$0.6	4%	$3.0	3%
Ophthalmology	$2.4	3%	$0.3	2%	$2.6	3%
Respiratory	$1.4	2%	$0.2	1%	$1.6	2%
Psychiatry	$1.4	2%	$0.1	1%	$1.5	2%
Platform	$0.2	0%	$0.0	0%	$0.2	0%
Total	**$85.3**	**100%**	**$14.2**	**100%**	**$99.6**	**100%**

Figure A3. Ten-year totals, by disease, for follow-on public offerings (FOPOs).

OUT-LICENSING OF R&D-STAGE THERAPEUTICS FROM EMERGING COMPANIES, BY DISEASE, 2009-2018

R&D-Stage Licensing (>$10M)	U.S.		Europe		Asia		ROW		Global Total	
Oncology	338	30%	143	28%	40	30%	60	26%	581	29%
Neurology	114	10%	75	15%	20	15%	35	15%	244	12%
Infectious Disease	99	9%	49	10%	18	13%	27	12%	193	10%
Platform	102	9%	36	7%	4	3%	12	5%	154	8%
Other	86	8%	32	6%	10	7%	24	10%	152	8%
Immunology	84	7%	44	9%	10	7%	13	6%	151	8%
Endocrine	71	6%	22	4%	11	8%	19	8%	123	6%
Cardiovascular	52	5%	14	3%	5	4%	12	5%	83	4%
Metabolic	43	4%	14	3%	6	4%	11	5%	74	4%
Hematology	43	4%	7	1%	2	1%	4	2%	56	3%
Ophthalmology	32	3%	13	3%	2	1%	6	3%	53	3%
Respiratory	23	2%	26	5%	0	0%	1	0%	50	2%
Gastrointestinal	28	2%	16	3%	3	2%	5	2%	52	3%
Psychiatry	17	2%	17	3%	3	2%	4	2%	41	2%
Total	**1132**	**100%**	**508**	**100%**	**134**	**100%**	**233**	**100%**	**2007**	**100%**

Figure A4. R&D-stage licensing deals by disease and region for the decade 2009-2018. Total dollars include totals of upfront payments for transactions with potential disclosed values over $10 million. Market-stage deals have been excluded from this analysis, as they do not offer the best representation of current pipeline interests. Licensing deals involving marketed products tend to be for regional marketing rights and often have different characteristics than those found in R&D-stage deal terms.

AQUISITIONS OF R&D-STAGE THERAPEUTIC COMPANIES WORLDWIDE, BY DISEASE, 2009-2018

R&D-Stage ETC Acquistions	U.S.		Europe		Asia		ROW		Global Total	
Oncology	79	29%	28	26%	2	29%	10	32%	119	28%
Platform	33	12%	15	14%	1	14%	4	13%	53	13%
Infectious Disease	27	10%	16	15%	1	14%	3	10%	47	11%
Neurology	28	10%	15	14%	1	14%	3	10%	47	11%
Immunology	16	6%	4	4%	0	0%	4	13%	24	6%
Other	17	6%	5	5%	1	14%	1	3%	24	6%
Endocrine	12	4%	6	6%	0	0%	4	13%	22	5%
Metabolic	13	5%	5	5%	0	0%	0	0%	18	4%
Cardiovascular	13	5%	3	3%	0	0%	1	3%	17	4%
Respiratory	8	3%	4	4%	0	0%	1	3%	13	3%
Ophthalmology	11	4%	2	2%	0	0%	0	0%	13	3%
Hematology	7	3%	1	1%	1	14%	0	0%	9	2%
Gastrointestinal	7	3%	2	2%	0	0%	0	0%	9	2%
Psychiatry	4	1%	1	1%	0	0%	0	0%	5	1%
Total	**275**	**100%**	**107**	**100%**	**7**	**100%**	**31**	**100%**	**420**	**100%**

Figure A5. R&D-stage acquisitions, by disease and region, for the decade 2009-2018. Aggregated numbers for the total value of non-conditional (ex-CVR) acquisition cost (for deals with disclosed potential value above $10M). Some recent R&D-stage acquisitions have Contingent Value Rights (CVRs) built into the deal structure. These are not guaranteed funds and have thus been excluded from this analysis.

Bio Industry Analysis

For more reports from BIO's Industry Analysis team, please visit wwww.bio.org/iareports

Authors

David Thomas, CFA

Vice President, Industry Research & Analysis

Biotechnology Innovation Organization (BIO)

Chad Wessel

Senior Manager, Industry Research & Policy Analysis

Biotechnology Innovation Organization (BIO)

Acknowledgements

We would like to acknowledge BIO staff John Guy and Bernard Fallon for their review of this report.

www.bio.org/iareports