Emerging Therapeutic Company Investment and Deal Trends

US Venture Capital and Public Offerings, 2008-2017
Global Licensing and Acquisitions, 2008-2017
Current Pipeline for Emerging Companies

by David Thomas, CFA and Chad Wessel
BIO INDUSTRY ANALYSIS

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Letter from the Honorable Jim Greenwood & Dr. Cartier Esham

May 17, 2018

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, 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:** A record $7.8 billion in venture funding went to US emerging therapeutic companies in 2017, indicating a robust interest in early-stage biotech. Series A financing increased to a record $2.9 billion, driven mainly by investor interest in immuno-oncology.
- **IPOs:** The IPO market rebounded with 69% more raised across 25 IPOs in 2017 for emerging therapeutic companies.
- **Follow-On Public Offerings:** Public market follow-on offerings for R&D-stage emerging companies rebounded in 2017 (up 163% in dollars raised vs. 2016).
- **Licensing:** The number of R&D-stage licensing deals valued at $10 million or more increased 22% in 2017 vs. 2016.
- **Acquisitions:** The number of R&D-stage company acquisitions reached a decade low, in large part due to a decrease in oncology acquisitions. A single outlier acquisition (in oncology) pushed the total dollar amount up 32% in 2017 vs. 2016.
- **Pipeline:** Total active clinical-stage programs reached a record 6,679 with 71% of programs involving emerging companies.

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

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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. We define emerging companies as those with less than $1 billion in sales. More than 95% of emerging companies are R&D-stage without an FDA approved therapeutic product. Transactions in this report are detailed by clinical development stage and disease area of the lead product under development by the emerging company. In addition, clinical pipeline data for each disease area are provided to give context on the 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 analyzed the most recent 10 years of investment and deal activity 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, data was gathered from Nasdaq and S-1 filings with initial tracking from various news sources, including EndPoints, BioCentury, BioWorld, and FierceBiotech. Follow-on offering data uses BioCentury's BCIQ as the primary data set. 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 funding 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 offerings, financings that can provide timely access to capital after key clinical or regulatory milestones. All three events – venture financing, IPOs, and follow-on offerings – are impactful for emerging companies, and are captured in this report by both stage of development and lead therapeutic categories for US companies.

Licensing is also a significant source of funding for emerging companies, and often entails sharing of development expertise and technical resources with a larger company. The inclusion of company acquisitions in this study aims to shed light on where global drug developers are willing to go "all in" on innovation to complement their own pipelines. For both licensing and acquisitions, US and ex-US transactions are presented.

A Decade of Investment into US Emerging Therapeutic Companies (2008-2017)

Over the last decade, a total of $130 billion in investment dollars went to US emerging therapeutic companies through venture capital ($45.9 billion), initial public offerings ($18 billion), and follow-on public offerings ($65.8 billion).

TOTAL EMERGING THERAPEUTICS INVESTMENT AND DEAL-MAKING

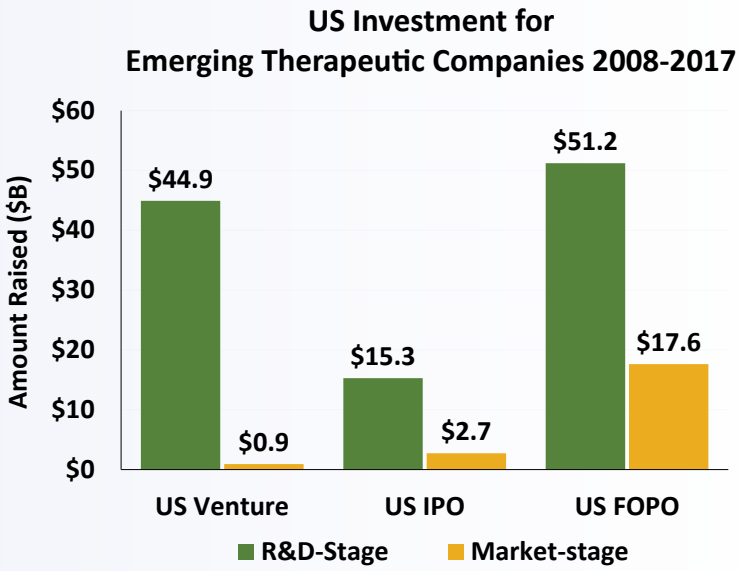


Chart 1. Investment into US emerging therapeutic companies 2008-2017.

A substantial amount of capital has flowed into emerging companies, but as can be seen in the following pages, investment since 2008 has been anything but steady. For example, during the 2008-2010 period, in the aftermath of the global financial crisis, companies struggled to source new capital from public markets and IPOs and follow-on offerings reached new lows. The stock market environment should also be noted for context during this timeframe. From January 1, 2008 through December 31, 2017, the Nasdaq Biotechnology Index increased 302%, compared to the S&P500 gain of 82%, with much of these gains made in the post-2012 era.

A Decade of Global Deal-Making with Emerging Therapeutic Companies (2008-2017)

Total licensing upfront payments over the last decade totaled $41.4 billion across 1,254 deals with disclosed values of $10 million or more (our proxy for corporate deal activity). This includes 44 "blockbuster" deals (those with potential amounts greater than $1B), and 30 alliances formed in just the last two years. Acquisitions of R&D-stage companies totaled $116.6 billion in upfront cash for 298 companies. For Market-stage emerging companies, $176.8 billion was spent on 126 companies. These robust deal-making and acquisition numbers and dollar amounts point to an ongoing strategic imperative for large companies to seek external innovation to fill their pipelines.

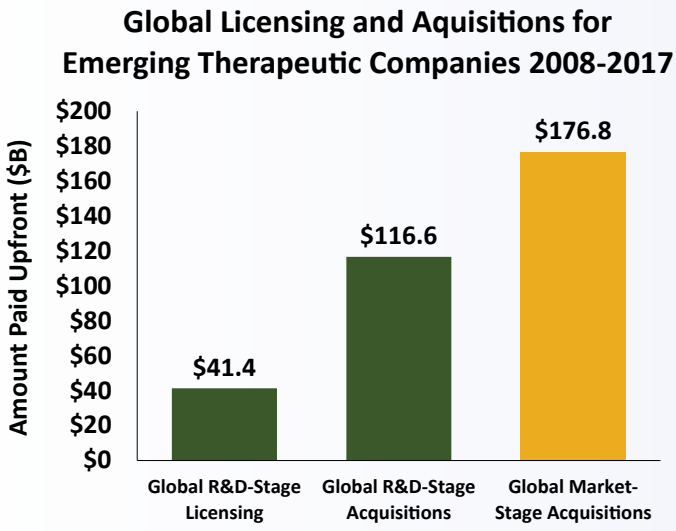


Chart 2. Breakdown of large biopharmaceutical company spending (as upfront payments) to access innovation through R&D-stage licensing deals, R&D-stage acquisitions, and Market-stage acquisitions of emerging biotech companies.

A Decade of US ETC Investment by Disease (2008-2017)

US Investment ($M) 2008-2017	US Venture		US IPO		US FOPO		Total	
Oncology	$13,138	29%	$4,382	24%	$19,216	29%	$36,736	28%
Infectious Disease	$4,960	11%	$1,503	8%	$9,523	14%	$15,986	12%
Neurology	$5,121	11%	$2,194	12%	$8,097	12%	$15,412	12%
Other	$3,359	7%	$2,327	13%	$4,100	6%	$9,786	8%
Metabolic	$2,446	5%	$1,030	6%	$4,934	7%	$8,410	6%
Endocrine	$3,421	7%	$764	4%	$3,905	6%	$8,090	6%
Hematology	$952	2%	$1,731	10%	$4,326	7%	$7,009	5%
Immunology	$2,040	4%	$667	4%	$3,283	5%	$5,990	5%
Cardiovascular	$1,724	4%	$948	5%	$2,591	4%	$5,263	4%
Ophthalmology	$1,908	4%	$1,064	6%	$1,963	3%	$4,935	4%
Platform	$4,191	9%	$475	3%	$155	0%	$4,821	4%
Gastrointestinal	$746	2%	$423	2%	$1,890	3%	$3,059	2%
Respiratory	$1,236	3%	$199	1%	$1,242	2%	$2,677	2%
Psychiatry	$619	1%	$299	2%	$610	1%	$1,528	1%
Total	$45,861	100%	$18,006	100%	$65,837	100%	$129,704	100%

Table 1. Ten-year totals, by disease, for US venture funding, initial public offerings (IPOs), and follow-on public offerings (FOPOs). The percentage indicates the proportion of total dollars raised. For FOPOs, the total dollars include only transactions raising over $10 million. Private Investments in Public Equity (PIPEs), such as Registered Direct Offerings to a single investor, are not included in this post-IPO offering analysis. However, the analysis of FOPOs here is intended to capture the broad, public investment sentiment in the sector. As there are big swings during the decade shown, we refer readers to the detailed year by year tables to assess disease area fund flow.

A Decade of Global Deals by Disease (2008-2017)

Global Deals ($M) 2008-2017	Licensing R&D-Stage		Acquistions R&D-Stage		Acquistions Market-Stage		Total	
Oncology	$14,465	35%	$37,641	33%	$79,177	45%	$131,283	40%
Other	$2,359	6%	$3,687	3%	$32,539	18%	$38,585	12%
Infectious Disease	$2,121	5%	$23,015	20%	$5,791	3%	$30,928	9%
Immunology	$3,051	7%	$4,278	4%	$18,944	11%	$26,273	8%
Gastrointestinal	$1,652	4%	$8,769	8%	$12,174	7%	$22,596	7%
Neurology	$4,659	11%	$8,717	8%	$3,744	2%	$17,121	5%
Endocrine	$2,564	6%	$5,191	5%	$8,768	5%	$16,524	5%
Metabolic	$1,969	5%	$10,370	9%	$1,760	1%	$14,100	4%
Respiratory	$1,140	3%	$2,070	2%	$8,375	5%	$11,585	4%
Cardiovascular	$1,950	5%	$1,983	2%	$1,818	1%	$5,750	2%
Platform	$2,484	6%	$2,512	2%	$0	0%	$4,996	2%
Hematology	$1,028	2%	$2,225	2%	$1,634	1%	$4,887	1%
Ophthalmology	$1,224	3%	$1,374	1%	$561	0%	$3,158	1%
Psychiatry	$711	2%	$788	0.7%	$1,214	0.7%	$2,713	1%
Total	$41,377	100%	$112,619	100%	$176,500	100%	$330,497	100%

Table 2. Ten-year totals, by disease, for R&D-stage licensing, R&D-stage acquisitions, and marketed product-stage acquisitions. The percentage indicates the proportion of total dollars raised. Total dollars include totals of upfront payments for transactions with potential disclosed values over $10 million. There are two major differences between R&D-stage and marketed product-stage deals. 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. Such deals have been excluded from this analysis, as they do not offer the best representation of pipeline interests, nor the bulk of the needs of emerging companies. For acquisitions, R&D-stage acquisitions tend to have Contingent Value Rights (CVRs) built in but are not guaranteed funds and have thus been excluded from this analysis.

Venture Capital Funding of US Therapeutic Companies

As shown in **Chart 3**, venture capital funding of private drug development reached a decade high of $7.8 billion in 2017. This is a $0.8 billion increase from the prior peak reached in 2015 ($7 billion). As was the case in 2016, the top quartile of companies received 70% of all venture funding in 2017. The top three companies raised nearly $1 billion combined, and eleven companies raised more than $100 million each. This illustrates that much of the increase in invested dollars ends up funding a small group of companies.

We categorized venture capital 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 examines innovative, unique, and potentially disease-modifying agents for diseases with current unmet medical need. Improvements include new delivery methods, new formulations, or using approved drugs for new indications. The majority of venture funding continues to flow into novel drug R&D, reaching a peak of 92% in 2015 and down slightly to 88% in 2017.

With respect to phase of development, the early stages (Preclinical and Phase I) continue to receive more funding vs. late stage from venture capital investment. Early-stage financing has increased from just above 58% of total funding in the 2008-2016 period to 64% in 2017.

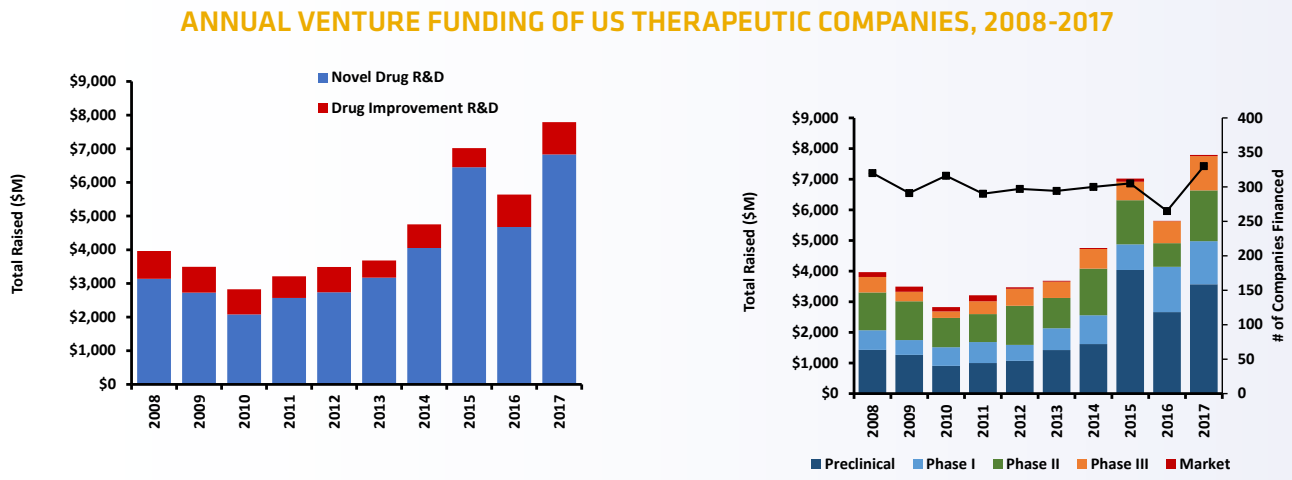


Chart 3. Total venture funding from 2008-2017. Left: Funding is represented as investment toward R&D of novel molecular entities vs. R&D for improvements of approved drugs (including delivery and reformulation). Right: Total venture funding by Phase of Development with the number of companies financed by year.

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.

Venture Funding of US Therapeutic Companies by Disease in 2017

As a percentage of total venture capital tracked, 37% went into oncology in 2017, an increase from annual average allocations since 2008 and the highest by far of all 12 disease areas tracked. As can be seen in **Chart 4**, a record 113 oncology companies received $2.9 billion in venture financing. This towers over the second most funded category, infectious disease, raising $959 million in 2017, and is 162% more in number than neurology's record 43 companies receiving venture financing.

Infectious disease experienced a large increase in funding in 2017 primarily due to a single company bringing in $500 million. Neurology's interest spanned nine pain companies, eight Alzheimer's companies, and 26 companies working on indications such as epilepsy and various rare diseases. One company in Phase III testing of products for Type 2 Diabetes received $340 million.

Endocrine-focused venture financing came off record highs seen in 2016, though that was primarily driven by a single company. The metabolic disease category saw a major increase in both dollars and number of transactions in 2017. Funding increased from $176 million to $379 million and the number of companies receiving funds increased from 10 in 2016 to 16 in 2017, with 14 of the 16 companies lead products being developed for rare genetic diseases.

Companies with lead programs in psychiatry, hematology, cardiovascular, and gastrointestinal diseases received the least amount of funding in 2017, with each category receiving well under $150 million. Psychiatry venture funding hit a decade low.

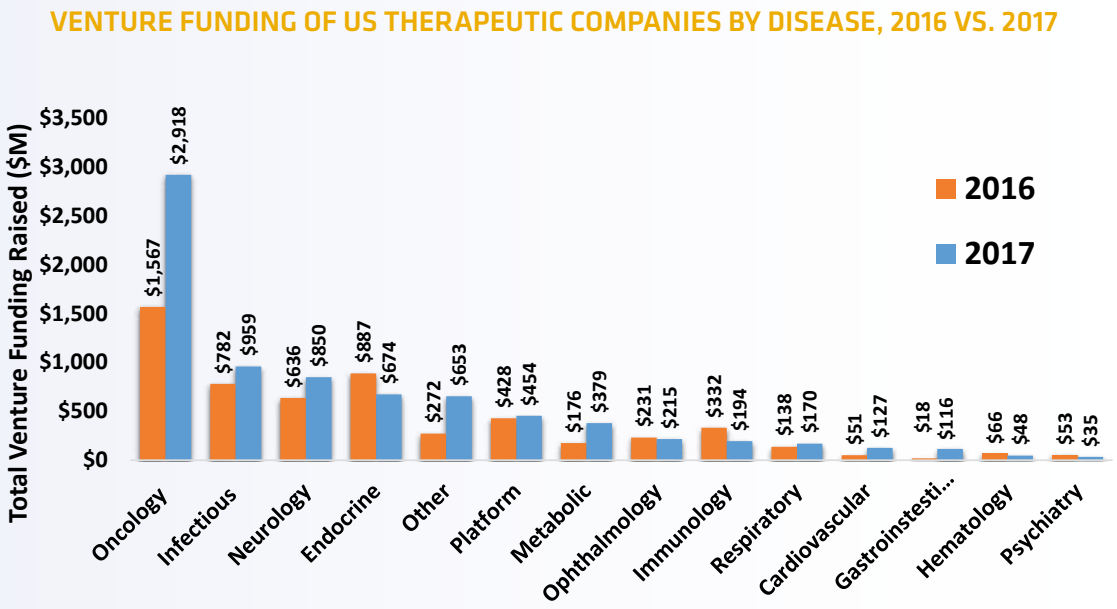


Chart 4. Total venture funding in 2016 and 2017 by disease, sorted highest to lowest funding in 2017.

US Venture Funding by Disease, 2008-2017

Table 3 shows the number of deals and the total dollar amount invested in each disease area each year, as well as a comparison of the two five-year periods. The totals include both novel drug and drug improvement funding.

Most of the disease categories show an increase in funding for the most recent five-year period. Part of this is explained by the prior five-year period (2008-2012) spanning the worldwide financial crisis, while the most recent period (2013-2017) aligned with economic recovery and a return of the public markets, renewed interest in biotechnology due to landmark drug approvals for public biopharmaceutical companies, and significant changes at the regulatory level. For example, the PUDFA V agreement launched the Breakthrough Therapy Designation, and the JOBS act of 2012 spurred >200 IPOs during this latter time-frame. More recently, the 21st Century Cures Act and the PDUFA VI agreement have been positive for innovation in the industry.

However, cardiovascular, gastrointestinal, and hematology saw less funding over this period, and respiratory and psychiatry remained at low levels. Platform and oncology companies saw the largest increase in dollars invested.

In **Chart 5**, venture investment into each disease area is displayed by novel drug R&D and drug improvement R&D investment. Over the last decade, endocrine and neurology have experienced a much higher percentage in drug improvement R&D investment than most other disease areas. In contrast, oncology and metabolic continue to have mostly novel R&D investment.

ANNUAL VENTURE FUNDING OF US THERAPEUTIC COMPANIES BY DISEASE, 2008-2017

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	69	64	64	74	75	63	80	87	94	113	346	437
Neurology	36	41	42	40	41	39	35	39	34	43	200	190
Infectious	36	37	43	34	20	33	34	30	30	32	170	159
Other	29	25	34	19	24	26	27	30	19	36	131	138
Platform	35	24	32	23	27	29	36	22	22	16	141	125
Endocrine	19	19	17	18	16	17	12	17	15	18	89	79
Ophthalmology	11	18	15	15	13	21	15	12	12	14	72	74
Metabolic	9	11	11	13	18	13	11	17	10	16	62	67
Immunology	23	14	11	8	12	10	15	10	8	11	68	54
Cardiovascular	19	15	18	18	16	16	12	12	3	7	86	50
Respiratory	14	9	11	10	7	8	8	13	8	10	51	47
Hematology	8	6	10	7	11	7	5	7	4	2	42	25
Psychiatry	2	5	4	6	10	7	6	4	3	5	27	25
Gastroinstestinal	10	3	4	4	8	5	4	5	3	7	29	24
Total	320	291	316	289	298	294	300	305	265	330	1514	1494

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	$1,136	$919	$616	$923	$740	$1,042	$1,225	$2,053	$1,567	$2,918	$4,333	$8,805
Neurology	$453	$532	$314	$184	$322	$375	$456	$1,000	$636	$850	$1,805	$3,316
Infectious	$435	$452	$323	$383	$167	$350	$535	$574	$782	$959	$1,760	$3,200
Platform	$180	$221	$250	$141	$286	$341	$874	$1,015	$428	$454	$1,077	$3,113
Endocrine	$209	$176	$77	$279	$284	$157	$305	$372	$887	$674	$1,025	$2,396
Other	$271	$225	$320	$206	$367	$283	$333	$429	$272	$653	$1,389	$1,970
Metabolic	$93	$162	$176	$241	$371	$265	$161	$422	$176	$379	$1,043	$1,403
Immunology	$310	$157	$152	$57	$148	$171	$262	$258	$332	$194	$824	$1,217
Ophthalmology	$138	$196	$92	$216	$107	$275	$272	$166	$231	$215	$748	$1,159
Cardiovascular	$221	$167	$141	$256	$283	$177	$56	$245	$51	$127	$1,068	$656
Respiratory	$169	$106	$154	$106	$65	$60	$59	$210	$138	$170	$600	$636
Hematology	$109	$90	$104	$91	$150	$90	$42	$162	$66	$48	$544	$409
Psychiatry	$36	$50	$39	$58	$111	$44	$154	$39	$53	$35	$293	$326
Gastroinstestinal	$207	$39	$67	$66	$87	$52	$18	$76	$18	$116	$466	$280
Total	$3,964	$3,491	$2,826	$3,207	$3,488	$3,682	$4,753	$7,020	$5,637	$7,793	$16,977	$28,885

Table 3. Total number of venture capital deals for each disease group as well as the amount invested by disease from 2008-2017.

Annual US Venture Capital by Disease Area, 2008-2017

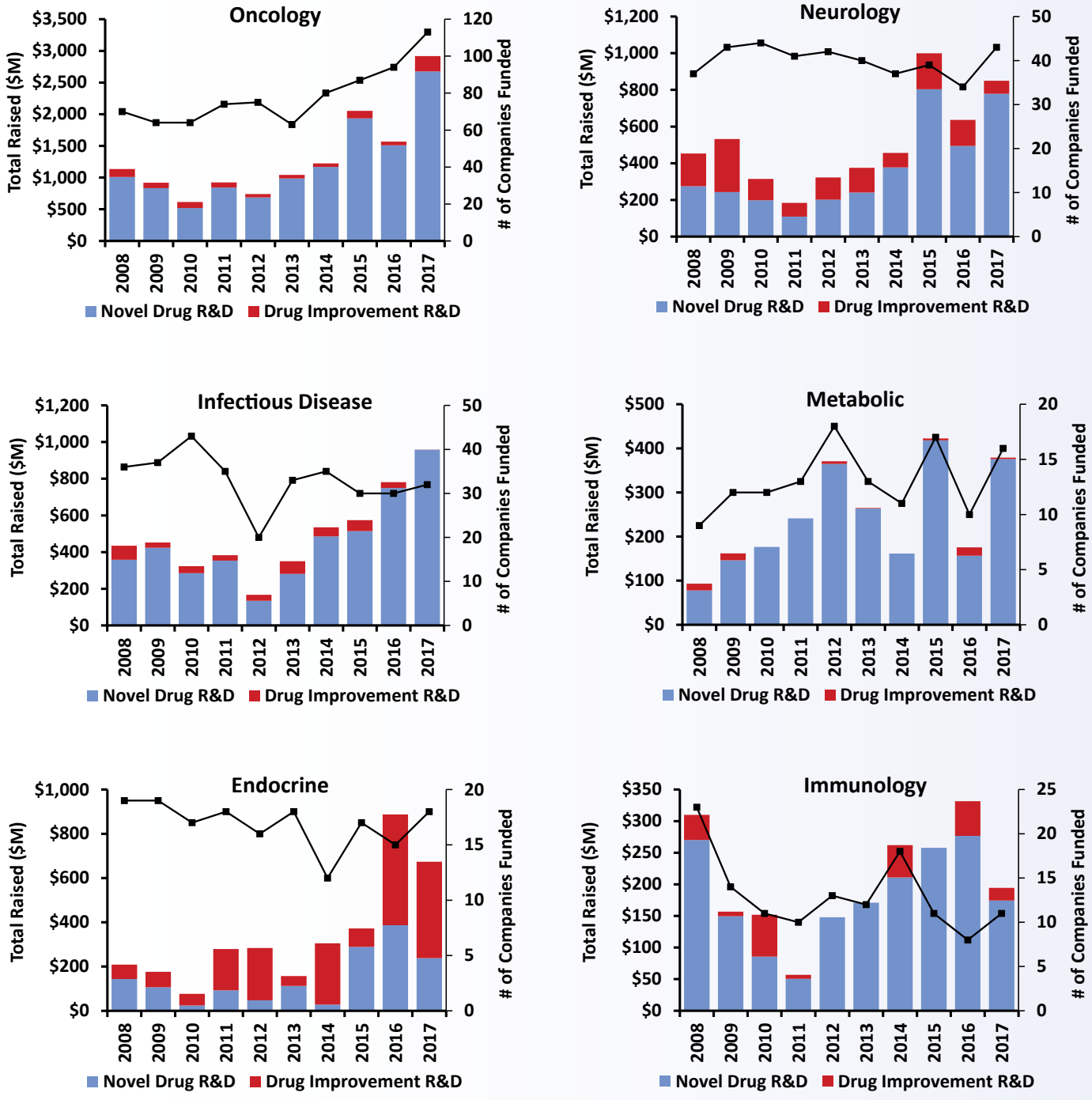


Chart 5. Total venture funding for each major disease area from 2008-2017. Funding is represented as investment toward R&D of novel molecular entities (blue) vs. improvements of approved drugs (red).

Annual US Venture Capital by Disease Area, 2008-2017

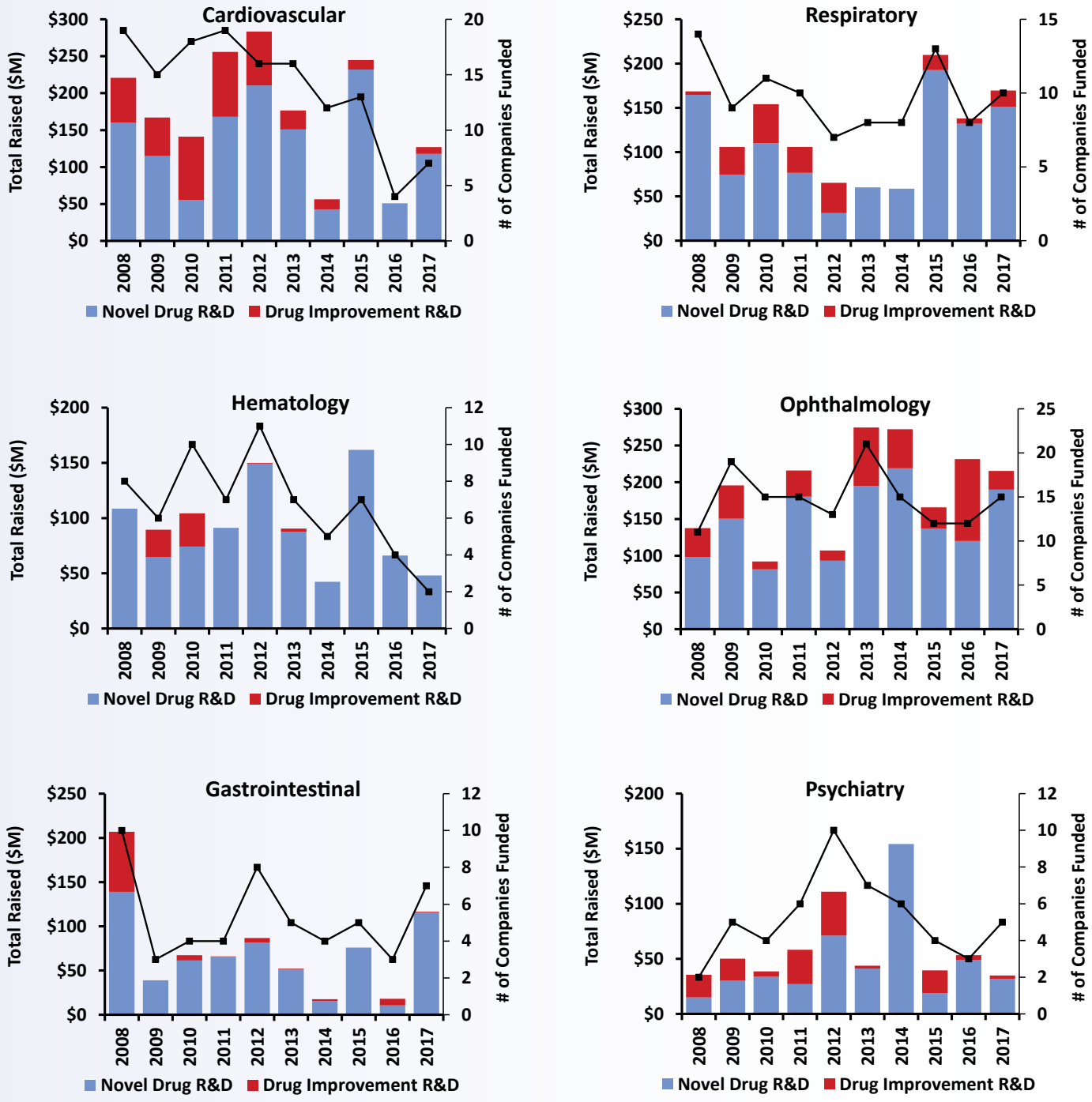


Chart 5. Total venture funding for each major disease area from 2008-2017. Funding is represented as investment toward R&D of novel molecular entities (blue) vs. improvements of approved drugs (red).

Series A Venture Funding of US 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 2017, a record amount was raised in Series A rounds, with nearly $2.9 billion going to early-stage companies. Over the last 10 years, Series A has accounted for 31% of all venture investment, but in 2017 this increased to 38%, indicating a shift toward more money going toward earlier stage investment. Preclinical companies took in 67% of all Series A venture dollars in 2017, above the decade average of 64%. Almost all Series A funding went into novel drug R&D, with only 6% invested into drug improvement R&D.

Series A rounds have increasingly been "tranched", meaning the total sum for an A round may come across long periods of time in separate payments dependent on company progress. Although the total number of companies receiving Series A across all tranches increased in 2017, the number of "first-time" Series A financings (A-1 rounds) increased slightly to 85 in 2017, from 80 in 2016. The limited increase in the number of companies funded combined with and an increase in funding has led to a boost in the average amount raised per Series A-1 round to $26.9 million vs. $18.6 million in 2017 vs. 2016. These averages have increased in recent years from the lows seen in 2008-2011 when averages were below $10 million.

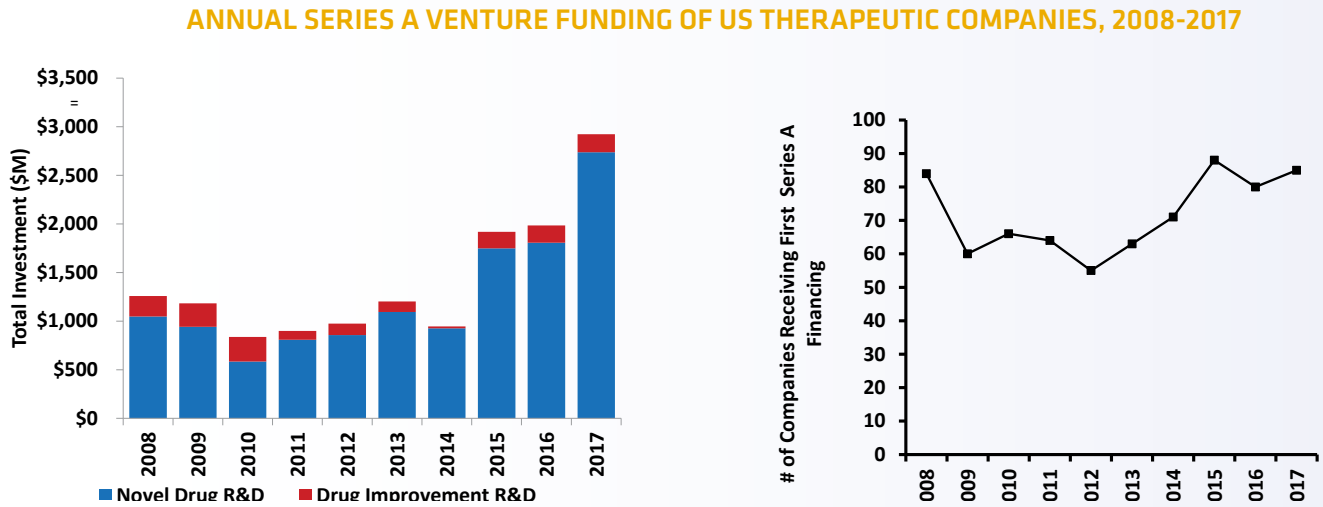


Chart 6. Left: Series A venture funding ($M) from 2008-2017. Funding is represented as investment toward R&D of novel molecular entities (blue) vs. improvements of approved drugs (red). Right: Number of companies receiving their First Series A Round (A-1 rounds), 2008-2017.

Series A Venture Funding by Disease

Oncology Series A financing reached record levels in 2017, with $896 million funding 46 companies. This represents 35% of all Series A transactions for emerging therapeutic companies.

As seen in **Table 4**, slightly more neurology companies were funded in 2017 (18) vs. 2016 (14), but with significantly more money ($514 million vs. $177 million). Nine of these companies received their first tranche of Series A financings in 2017. Platform companies represented the third highest category in terms of number of companies (15) receiving Series A funding in 2017. Only three of the fifteen platform companies received their first Series A tranche in 2017.

Six disease categories, of the 14 listed in **Table 4,** raised less than $100 million each in 2017. Endocrine and cardiovascular companies raised $93 and $72, respectively. Hematology, metabolic, ophthalmology, and psychiatry were the bottom four disease areas in terms of Series A financing in 2017, with each receiving under $50 million. For ophthalmology and psychiatry, this is consistent with past years. Hematology and psychiatric disease areas each saw only one company receive financing.

Annual Series A Venture Funding by Disease, 2008-2017

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	29	21	21	30	23	24	29	49	54	49	124	205
Neurology	13	21	18	20	20	16	13	16	18	22	92	85
PLATFORM	16	11	13	7	10	17	18	12	15	10	57	72
Infectious Disease	18	12	17	9	9	10	10	14	11	11	65	56
Other	13	11	15	9	10	11	10	10	8	15	58	54
Endocrine	8	5	6	8	7	4	4	7	5	8	34	28
Metabolic	4	4	4	5	6	2	2	7	4	9	23	24
Ophthalmology	7	6	8	6	7	7	3	3	4	5	34	22
Cardiovascular	7	6	8	8	7	6	5	5	1	3	36	20
Hematology	6	4	5	1	4	3	3	3	4	1	20	14
Immunology	11	7	3	6	4	2	3	1	3	4	31	13
Respiratory	7	3	6	4	1	2	3	2	1	4	21	12
Psychiatry	0	1	2	3	4	4	1	3	2	1	10	11
Gastrointestinal	5	2	3	0	2	1	0	2	2	4	12	9
Total	144	114	129	116	114	109	104	134	132	146	617	625

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	$290	$324	$135	$250	$99	$372	$251	$733	$778	$957	$1,098	$3,091
Neurology	$107	$226	$121	$84	$123	$162	$163	$392	$269	$559	$660	$1,546
PLATFORM	$98	$113	$98	$47	$152	$215	$228	$174	$277	$314	$507	$1,209
Infectious Disease	$173	$86	$37	$118	$56	$88	$87	$169	$57	$248	$471	$649
Other	$121	$98	$126	$67	$82	$95	$39	$60	$142	$143	$493	$479
Metabolic	$23	$28	$13	$79	$80	$28	$18	$135	$81	$177	$223	$439
Ophthalmology	$71	$49	$45	$92	$59	$113	$26	$28	$32	$111	$317	$309
Endocrine	$48	$47	$12	$12	$29	$5	$19	$65	$68	$93	$148	$251
Cardiovascular	$39	$41	$38	$22	$133	$44	$18	$54	$50	$72	$273	$238
Hematology	$40	$26	$45	$2	$54	$35	$37	$21	$66	$45	$166	$204
Gastrointestinal	$48	$9	$64	$0	$16	$15	$0	$27	$11	$115	$137	$167
Immunology	$150	$115	$16	$50	$51	$10	$44	$7	$63	$41	$382	$164
Respiratory	$52	$22	$62	$50	$3	$0	$8	$34	$45	$34	$188	$121
Psychiatry	$0	$2	$25	$24	$39	$20	$7	$19	$45	$14	$91	$104
Total	$1,259	$1,183	$838	$898	$975	$1,202	$945	$1,919	$1,984	$2,923	$5,154	$8,973

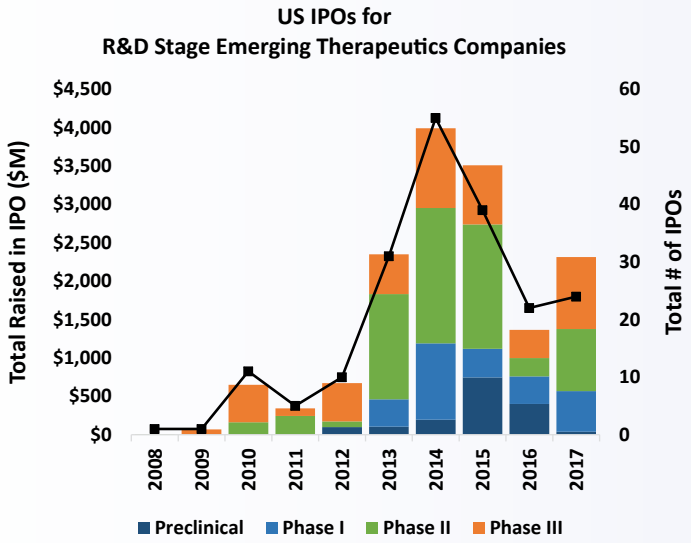
Table 4. Series A venture funding ($M) and number of venture transactions by disease area, 2008-2017

Initial Public Offerings from US Therapeutic Companies

Public financing of US emerging therapeutic companies showed little increase in the number of transactions in 2017, with 25 initial public offerings (IPOs) versus the 23 seen in 2016. Although the number of companies did not increase significantly, the amount raised increased dramatically to $2.4 billion in 2017 versus $1.4 billion in 2016. Of the $2.4 billion raised, 75 percent of the money invested was in late stage companies (Phase II & III). This is considerably more than 2016, which saw 42 percent of the IPOs in late stage development.

The average amount raised per IPO for R&D-stage companies was $96 million in 2017, the highest amount seen over the 10-year period, 2008-2017. Although the number of Preclinical and Phase I companies going public was greatly reduced in 2017 compared to 2016 (from 13 to 5), the average amount raised per company increased to $114 million in 2017 from $58 million in 2016.

ANNUAL IPOS FOR US R&D-STAGE THERAPEUTIC COMPANIES, 2008-2017



Stage at time of IPO	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Preclinical - Phase III (#)	1	1	11	5	10	31	55	39	22	24
Marketed (#)	0	2	1	3	1	1	5	0	1	1
Total (#)	1	3	12	8	11	32	60	39	23	25
Preclinical - Phase III ($M)	$5	$68	$650	$343	$672	$2,350	$3,993	$3,508	$1,366	$2,314
Marketed ($M)	$0	$1,035	$56	$197	$55	$37	$1,161	$0	$75	$120
Total ($M)	$5	$1,103	$706	$541	$727	$2,387	$5,154	$3,508	$1,441	$2,434

Chart 7. Top: IPOs for US R&D-stage emerging therapeutic companies, by phase, 2008-2017. Bottom: The number of IPOs and total dollars raised via IPOs per year for R&D-stage and market-stage companies.

IPOs for US Therapeutic Companies, by Disease

2017 marked the return to dominance of oncology and neurology companies for R&D staged companies completing their IPO. In 2017, 11 out of the 25 companies had a lead product in these two areas, raising nearly 50 percent of the $2.4 billion raised through IPOs. This is a similar trend seen between 2011 and 2015. In 2016 metabolic, platform technologies, and the other disease category of companies raised the majority of funds with 50 percent of the capital raised.

ANNUAL IPOS FOR US THERAPEUTIC COMPANIES, BY DISEASE, 2008-2017

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	0	0	1	3	3	14	10	9	4	8	7	45
Neurology	0	1	2	2	1	0	8	11	0	3	6	22
Infectious Disease	0	0	3	0	2	4	8	2	3	2	5	19
Other	0	1	1	1	1	0	6	2	2	4	4	14
Metabolic	0	0	0	0	1	3	2	3	3	2	1	13
Cardiovascular	1	0	2	0	0	2	3	3	2	2	3	12
Ophthamology	0	0	1	0	0	2	4	2	1	2	1	11
Endocrine	0	0	0	0	0	0	8	2	0	0	0	10
Hematology	0	1	0	0	0	3	3	2	0	1	1	9
Inflammation	0	0	1	1	2	1	4	0	2	0	4	7
Platform	0	0	0	0	1	1	2	0	3	0	1	6
Psychiatry	0	0	0	0	0	0	1	2	0	1	0	4
Gastrointestinal	0	0	1	1	0	1	1	0	2	0	2	4
Respiratory	0	0	0	0	0	1	0	1	1	0	0	3
Total	1	3	12	8	11	32	60	39	23	25	35	179

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	$0	$0	$81	$248	$236	$958	$1,033	$897	$162	$766	$565	$3,817
Other	$0	$85	$30	$106	$81	$0	$1,212	$215	$263	$335	$302	$2,025
Neurology	$0	$68	$106	$82	$55	$0	$467	$1,058	$0	$358	$311	$1,883
Infectious Disease	$0	$0	$123	$0	$140	$315	$420	$211	$178	$117	$263	$1,241
Ophthamology	$0	$0	$72	$0	$0	$234	$267	$201	$50	$240	$72	$992
Metabolic	$0	$0	$0	$0	$50	$301	$176	$155	$189	$160	$50	$980
Cardiovascular	$5	$0	$90	$0	$0	$134	$161	$253	$91	$215	$95	$853
Hematology	$0	$950	$0	$0	$0	$205	$309	$192	$0	$75	$950	$781
Endocrine	$0	$0	$0	$0	$0	$0	$612	$152	$0	$0	$0	$764
Inflammation	$0	$0	$17	$50	$120	$73	$302	$0	$105	$0	$187	$480
Platform	$0	$0	$0	$0	$45	$70	$102	$0	$258	$0	$45	$430
Psychiatry	$0	$0	$0	$0	$0	$0	$33	$98	$0	$168	$0	$299
Respiratory	$0	$0	$0	$0	$0	$72	$0	$77	$50	$0	$0	$199
Gastrointestinal	$0	$0	$188	$55	$0	$25	$60	$0	$95	$0	$243	$180
Total	$ 5	$ 1,103	$ 706	$ 541	$ 727	$ 2,387	$ 5,154	$ 3,508	$ 1,441	$ 2,434	$ 3,082	$ 14,924

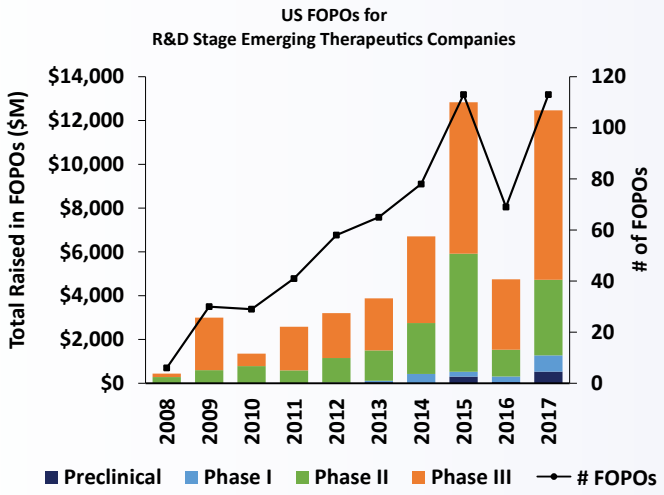
Table 5. IPOs by US emerging companies, 2008-2017. Amount raised ($M) and number of deals by disease. Listed by total number of deals in 2017, top to bottom.

Follow-On Public Offerings from US Therapeutic Companies

Capital raised via follow-on public offerings (FOPOs) nearly doubled in 2017 for US emerging companies at $13.9 billion, compared to the $7.1 billion raised in 2016. This marks the second highest amount seen in FOPO's over the last 10 years. This increase in capital raised was driven by R&D-stage companies. In 2017, Phase III companies raised the highest amount seen over the 10-year period with $7.7 billion. Companies with a marketed product are the only group to show a decrease in the amount raised in 2017. In fact, 2017 was the lowest year for Market-stage emerging companies of the last five years, with only $1.47 billion raised.

While 2017 is the second highest year in terms of the number of FOPO transactions (126), it is tied for the highest number of R&D stage companies completing a FOPO at 113 with 2015.

ANNUAL FOPOS FOR US THERAPEUTIC COMPANIES, 2008-2017



Stage at time of FOPO	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Preclinical - Ph III #, (>$10M)	6	30	29	41	58	65	78	113	69	113
Marketed #, ($>10M)	5	12	16	10	18	24	21	19	18	13
Total # (>$10M)	11	42	45	51	76	89	99	132	87	126
Preclinical - Ph III ($M)	$443	$2,996	$1,352	$2,583	$3,202	$3,876	$6,710	$12,831	$4,748	$12,467
Marketed ($M)	$580	$1,692	$1,281	$812	$1,647	$2,403	$2,147	$3,282	$2,314	$1,470
Total ($M)	$1,023	$4,688	$2,633	$3,395	$4,850	$6,279	$8,857	$16,113	$7,062	$13,936

Chart 8. Top: FOPOs for US R&D-stage emerging therapeutic companies, 2008-2017. Bottom: 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.

US Follow-On Public Offerings by Disease

Emerging oncology companies continue to raise the most capital through FOPOs ($3.8 billion) and had the most transactions (38) in 2017 vs. other disease groups, as they have consistently done over the 9 of the last 10 years. The only exception to this was 2015, when metabolic diseases companies focused on rare disorders raised the largest share of funding ($3.2 billion across 10 offerings).

While most disease groups showed a marked increase in amount financed between 2016 and 2017, only two diseases showed a decrease in funding through FOPO's in 2017, Gastrointestinal ($288 million to $123 million) and Endocrine ($239 million to $105 million). Companies with a lead product in respiratory disease raised the least of any disease category in 2017 (only $89 million). Psychiatric companies raised more in 2017 ($405 million) than the previous nine years combined.

ANNUAL US FOLLOW-ON PUBLIC OFFERINGS BY DISEASE, 2008-2017

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	2	15	11	19	28	25	30	38	23	38	75	154
Neurology	3	3	9	4	11	12	13	17	16	11	30	69
Infectious Disease	2	7	11	9	9	16	10	17	9	15	38	67
Other	0	1	0	2	2	7	8	10	9	12	5	46
Endocrine	1	2	4	5	6	8	5	13	4	3	18	33
Metabolic	1	3	0	3	6	2	8	10	4	8	13	32
Immunology	2	4	2	1	1	3	3	10	3	9	10	28
Hematology	0	1	2	2	1	4	5	4	4	11	6	28
Ophthalmology	0	2	1	0	4	1	4	7	7	4	7	23
Cardiovascular	0	0	3	2	3	3	6	5	2	5	8	21
Gastrointestinal	0	2	1	3	4	4	3	0	2	3	10	12
Respiratory	0	2	1	1	0	4	3	0	1	2	4	10
Psychiatry	0	0	0	0	1	0	1	1	3	3	1	8
Platform	0	0	0	0	0	0	0	0	0	2	0	2
Total	11	42	45	51	76	89	99	132	87	126	225	533

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	$174	$1,570	$644	$1,518	$1,782	$2,260	$2,090	$3,246	$2,093	$3,839	$5,688	$13,528
Metabolic	$81	$173	$0	$170	$662	$254	$949	$3,329	$436	$1,880	$1,086	$6,848
Neurology	$242	$115	$463	$238	$531	$423	$1,712	$1,792	$1,669	$913	$1,589	$6,508
Infectious Disease	$338	$1,765	$512	$572	$613	$1,049	$1,054	$1,863	$641	$1,117	$3,800	$5,724
Hematology	$0	$86	$270	$63	$18	$203	$403	$547	$460	$2,276	$437	$3,889
Other	$0	$109	$0	$46	$70	$418	$646	$1,071	$401	$1,340	$225	$3,876
Endocrine	$51	$181	$140	$249	$657	$538	$255	$1,491	$239	$105	$1,278	$2,627
Immunology	$139	$244	$241	$58	$38	$175	$334	$1,215	$286	$556	$719	$2,565
Cardiovascular	$0	$0	$76	$91	$114	$270	$345	$988	$86	$622	$281	$2,310
Ophthalmology	$0	$155	$62	$0	$146	$11	$284	$442	$345	$518	$363	$1,600
Gastrointestinal	$0	$190	$111	$294	$197	$342	$345	$0	$288	$123	$792	$1,098
Respiratory	$0	$100	$114	$96	$0	$337	$432	$0	$75	$89	$309	$933
Psychiatry	$0	$0	$0	$0	$22	$0	$11	$130	$44	$405	$22	$588
Platform	$0	$0	$0	$0	$0	$0	$0	$0	$0	$155	$0	$155
Total	$1,023	$4,688	$ 2,633	$3,395	$4,850	$6,279	$8,857	$16,113	$7,062	$13,936	$16,589	$52,248

Table 6. FOPOs, 2008-2017. Amount raised ($M) and number of deals by disease. Listed by total number of deals in 2017, top to bottom.

Global R&D-Stage Licensing

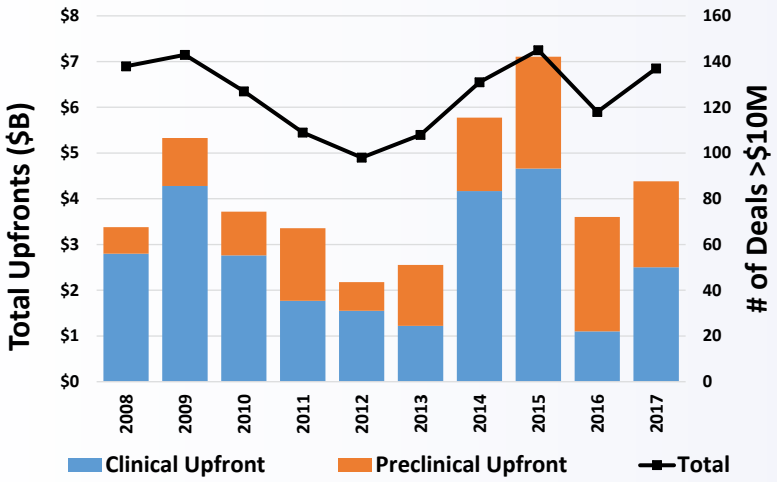
For licensing, we analyzed R&D-stage asset out-licensing activity by emerging companies for deals valued at >$10 million to best represent deal flow and interest from large biopharmaceutical players. Globally, there was a 16% increase in the number of out-licensing deals from 118 in 2016 to 137 in 2017. The aggregate dollar amount paid upfront to small companies for out-licensed programs increased by 22% from $3.6 billion in 2016 to $4.4 billion in 2017. As seen in **Chart 9**, both the number of deals and the total upfront dollar amounts for 2017 are below peak levels of 2015, but rank 4th highest for 2017 over the last 10 years of deal making.

US company assets remained the most sought-after assets for licensing, with 57% of 2017 ETC out-licensed deals. European asset out-licensing accounted for 28% and Asia 11% in 2017. Canadian assets made up the remaining 2%.

Although the majority of the 137 deals in 2017 were Preclinical-stage (66), on a percentage basis this was the lowest in seven years (48%). The aggregate upfront amount for these Preclinical-stage deals fell 25%, as did the aggregate potential milestones structured in these deals. However, the number of blockbuster Preclinical-stage deals (total potential value >$1 billion) matched the record 15 set in 2016, well above previous highs (prior to 2016 the previous high was four). Median Preclinical-stage upfront payment was $26 million and a median potential amount of $268 million.

Making up for the overall lag seen in Preclinical-stage deal values, was a rise in the Clinical-stage potential deal value. Clinical-stage deals jumped 58% in number and the total dollars from upfront payments increased 127%. The primary driver was Phase I oncology deals. The median Clinical-stage upfront payment was $20 million and a median total potential amount of $175 million.

ANNUAL GLOBAL LICENSING OF R&D-STAGE THERAPEUTICS, 2008-2017



Stage at Acquisition	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
R&D-stage	36	29	27	27	24	32	33	32	37	21
Market-stage	15	10	13	15	16	17	11	12	7	10
Total	51	39	40	42	40	49	44	44	44	31
R&D-stage Upfront ($M)	$6,203	$4,923	$5,777	$15,250	$6,627	$6,182	$9,979	$26,716	$13,321	$17,640
Market-stage Upfront ($M)	$19,680	$9,630	$11,598	$3,396	$16,390	$25,096	$19,285	$35,887	$22,165	$13,625
Total	$25,883	$14,553	$17,375	$18,646	$23,017	$31,278	$29,265	$62,603	$35,486	$31,266

Chart 9. Global licensing for R&D-stage emerging therapeutics, 2008-2017. Total upfront dollars per year for Preclinical and Clinical-stage assets plotted as bars with values on the left y-axis. The number of licensing deals (with values above $10M) is plotted as a line with values on the second y-axis.

ANNUAL GLOBAL LICENSING OF R&D-STAGE THERAPEUTICS, BY PHASE, 2008-2017

Number of Deals >$10M	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Preclinical	62	60	61	65	50	63	69	79	73	66	298	350
Phase I	21	15	10	10	13	14	16	16	9	21	69	76
Phase II	25	33	35	21	22	21	28	31	21	23	136	124
Phase III	30	35	21	13	13	10	18	19	15	27	112	89
Total	138	143	127	109	98	108	131	145	118	137	615	639

Upfront Amounts for Deals >$10M	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Preclinical	$582	$1,052	$955	$1,584	$626	$1,334	$1,601	$2,442	$2,505	$1,880	$4,799	$9,762
Phase I	$591	$547	$148	$172	$226	$462	$463	$1,816	$36	$664	$1,684	$3,442
Phase II	$700	$1,507	$1,989	$629	$867	$508	$1,530	$1,803	$598	$1,225	$5,692	$5,665
Phase III	$1,507	$2,223	$627	$970	$459	$249	$2,178	$1,044	$465	$612	$5,787	$4,547
Total	$3,381	$5,330	$3,719	$3,355	$2,177	$2,553	$5,772	$7,105	$3,604	$4,381	$17,962	$23,416

Total Potential Deal Amounts for Deals >$10M	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Preclinical	$7,793	$10,869	$18,198	$14,085	$13,777	$15,235	$17,247	$29,671	$45,118	$34,122	$64,723	$141,394
Phase I	$5,742	$5,204	$2,458	$4,144	$2,831	$8,016	$3,494	$8,604	$1,481	$10,302	$20,379	$31,897
Phase II	$4,801	$8,708	$13,407	$6,360	$5,724	$4,368	$10,764	$13,009	$6,803	$5,660	$38,999	$40,604
Phase III	$7,217	$8,214	$4,143	$5,224	$3,370	$1,700	$9,585	$4,921	$2,958	$5,025	$28,168	$24,190
Total	$25,552	$32,994	$38,207	$29,813	$25,702	$29,320	$41,091	$56,206	$56,360	$55,108	$152,269	$238,084

Table 7. Global licensing for R&D-stage emerging therapeutics, 2008-2017, by Phase. Top: The number of licensing deals (with values above $10M) by phase. Center: Total upfront dollars per year for R&D-stage assets, by phase. Bottom: Total potential amounts by phase (biobuck amounts combine upfront and total milestone payments).

Global R&D-Stage Licensing by Disease

Oncology R&D-stage out-licensing deals maintained their dominance across all phases and all disease areas in 2017. The number of deals valued at above $10 million for oncology reached 47, almost quadruple than the next highest number of deals in a disease category (Neurology had 12 deals). Although this is slightly less than 2016's 53 deals, the aggregate upfront payments for oncology came in at $2.3 billion in 2017, the second highest level of the decade. The last five years have seen an aggregate of more than $10 billion upfront payments, a 141% increase vs. the prior five-year period. Much of the renewed interest is centered on combination testing within existing immuno-oncology products (mainly anti-PD1/L1 biologics) but also new targets being tested independently.

As has been the case for the last nine years, Neurology was the second most active disease area in terms of deal volume with 12 R&D-stage deals. Upfront payments in Neurology came in at $385 million, above the previous two years ($327 and $229 million for 2015 and 2016, respectively). The majority of this came from Preclinical-stage deals in Neurodegenerative assets and platform technologies.

Immunology deals outnumbered Platform deals in 2017, a reversal from 2016. Endocrine and Infectious Disease also had a sizable change in the number of deals, moving from three each in 2016 to nine and seven deals, respectively, for 2017. Platform deals were spread across *in silico*/AI drug design companies, drug delivery, and novel biologics platforms. The deals in the "other" category were largely for assets within dermatology and sexual dysfunction. Marginal increases were seen in most of the remaining disease areas, with Gastrointestinal and Psychiatry deals remaining flat year over year for 2017.

GLOBAL LICENSING OF R&D-STAGE THERAPEUTICS BY DISEASE, 2016 VS. 2017

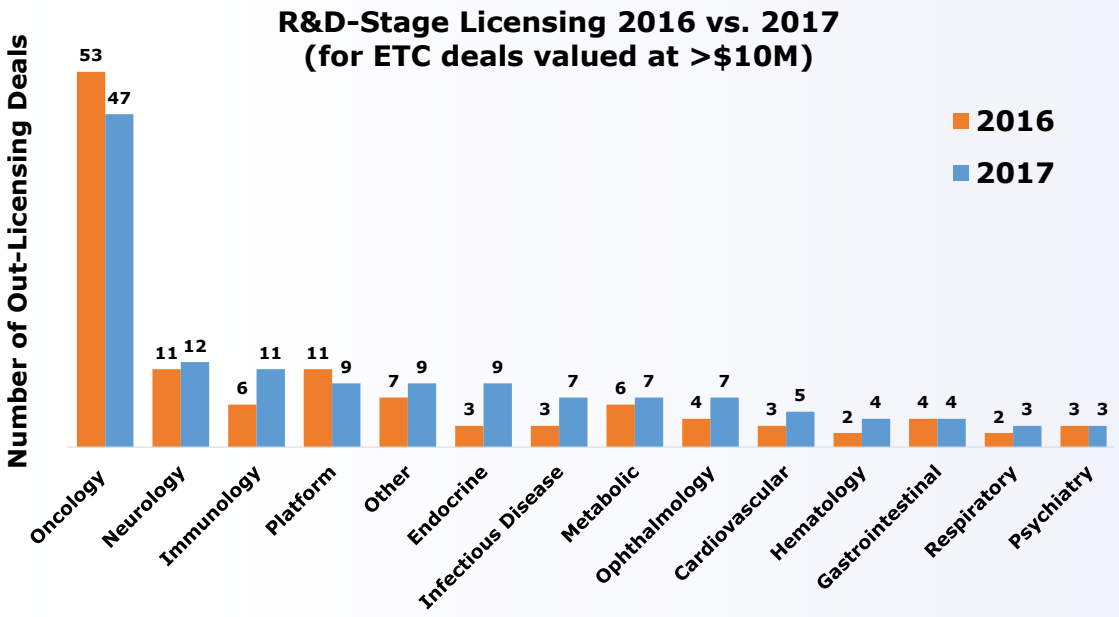


Chart 10. R&D-Stage Licensing in 2016 vs. 2017, by Disease Area, for deals with disclosed value above $10M. Deals are sorted highest to lowest by number of deals in 2017.

ANNUAL GLOBAL EMERGING COMPANY R&D OUT-LICENSING BY DISEASE, 2008-2017

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	30	33	26	36	25	33	52	58	53	47	150	243
Neurology	13	22	21	9	14	17	11	18	11	12	79	69
Platform	13	14	14	10	12	11	5	9	11	9	63	45
Other	14	5	10	10	12	7	13	9	7	9	51	45
Immunology	13	12	10	13	6	8	6	6	6	11	54	37
Endocrine	6	8	16	5	1	5	7	12	3	9	36	36
Infectious Disease	17	19	10	7	8	5	11	8	3	7	61	34
Metabolic	4	6	4	3	4	5	3	4	6	7	21	25
Cardiovascular	4	5	4	6	2	7	4	4	3	5	21	23
Ophthalmology	9	2	3	2	2	1	4	6	4	7	18	22
Hematology	5	4	2	2	4	5	4	5	2	4	17	20
Gastrointestinal	3	7	0	1	2	1	6	1	4	4	13	16
Respiratory	4	3	4	2	4	2	4	4	2	3	17	15
Psychiatry	3	3	3	3	2	1	1	1	3	3	14	9
Total	138	143	127	109	98	108	131	145	118	137	615	639

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	$841	$919	$533	$1,139	$804	$874	$1,697	$3,421	$1,981	$2,256	$4,236	$10,229
Neurology	$624	$1,589	$264	$128	$231	$296	$586	$327	$229	$384	$2,836	$1,823
Immunology	$233	$396	$189	$259	$163	$261	$82	$898	$259	$311	$1,240	$1,812
Platform	$270	$139	$230	$487	$71	$396	$142	$377	$234	$139	$1,197	$1,287
Endocrine	$138	$113	$476	$588	$8	$96	$530	$377	$92	$147	$1,323	$1,242
Metabolic	$272	$185	$166	$33	$95	$62	$738	$230	$120	$69	$751	$1,219
Gastrointestinal	$148	$266	$0	$50	$20	$70	$798	$0	$185	$116	$484	$1,169
Other	$138	$107	$681	$106	$310	$95	$152	$462	$195	$113	$1,342	$1,017
Ophthalmology	$53	$36	$25	$60	$163	$10	$418	$248	$51	$161	$336	$887
Hematology	$19	$102	$30	$25	$38	$66	$260	$230	$125	$133	$214	$814
Respiratory	$41	$275	$52	$9	$1	$50	$57	$380	$40	$234	$378	$762
Cardiovascular	$365	$175	$737	$72	$6	$120	$91	$82	$75	$227	$1,355	$595
Infectious Disease	$218	$797	$304	$197	$257	$58	$196	$65	$6	$24	$1,772	$349
Psychiatry	$22	$231	$32	$202	$11	$98	$25	$10	$13	$67	$498	$213
Total	$3,381	$5,330	$3,719	$3,355	$2,177	$2,553	$5,772	$7,105	$3,604	$4,381	$17,962	$23,416

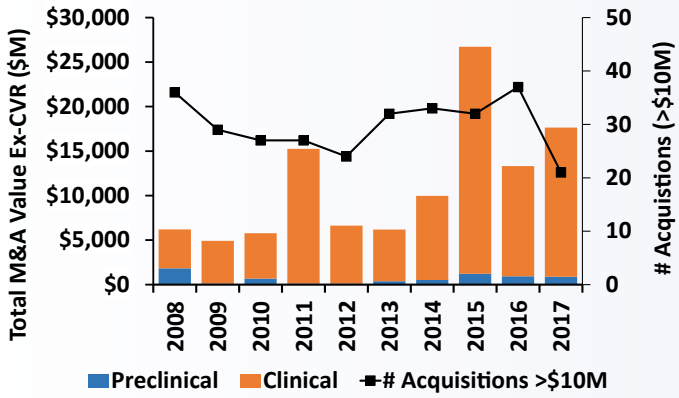
Table 8. Licensing, number of deals by disease and aggregate amount paid upfront ($M), 2008-2017, for deals with disclosed potential value above $10M.

Global Emerging Company Acquisitions

Global R&D-Stage ETC Acquisitions, 2008-2017

For R&D-stage buyouts, there was a dramatic drop in the number of acquisitions over the last two years, from 37 in 2016 to 21 in 2017. This represents the lowest number of acquisitions of R&D-stage therapeutic companies in more than a decade. Breaking the number of acquisitions down by phase indicates that the drop occurred for companies at all phases of development. The Kite acquisition by Gilead, for $11.9 billion, was an outlier among the R&D-stage acquisitions for 2017 making up 67% of the year's $17.6 billion in purchases. The median price paid for a R&D-stage company in 2017 was $137 million upfront and $425 million when all contingent payments are included. Excluding the Kite acquisition, the 2017 mean was $287 million upfront and $550 million when all contingent payments are included.

ANNUAL GLOBAL ACQUISITIONS OF R&D-STAGE THERAPEUTIC COMPANIES, 2008-2017



Stage at Acquisition	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Preclinical-stage	8	4	10	2	5	7	8	8	9	5
Clinical-stage	28	25	17	25	19	25	25	24	28	16
Total R&D-stage	36	29	27	27	24	32	33	32	37	21
Preclinical-stage Upfront ($M)	$1,831	$126	$686	$120	$124	$387	$523	$1,223	$941	$886
Clinical-stage Upfront ($M)	$4,372	$4,796	$5,091	$15,130	$6,503	$5,796	$9,457	$25,493	$12,381	$16,754
Total R&D-stage	$6,203	$4,923	$5,777	$15,250	$6,627	$6,182	$9,979	$26,716	$13,321	$17,640

Chart 11. Top: Acquisitions of global emerging therapeutic companies, by stage in R&D, 2008-2017. Bottom: The number of acquisitions (valued above $10M) and total dollars raised per year for R&D-stage companies.

Global Market-Stage ETC Acquisitions

Market-stage emerging therapeutic companies (those with sales below $1 billion) saw 10 companies acquired by larger biopharmaceutical companies for $13.9 billion, as shown in **Table 9**. This places the average acquisition price at the lowest in five years. It should be noted that the largest acquisition of the year, Actelion's $30 billion acquisition by JNJ, is not included as Actelion's 2016 sales were above the $1 billion threshold we use for "emerging" therapeutic-focused companies.

ANNUAL ETC ACQUISITIONS BY PHASE, 2008-2017

Number of Acquisitions >$10M	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Preclinical	8	4	10	2	5	7	8	8	9	5	29	37
Phase I	7	3	2	5	3	2	6	8	4	3	20	23
Phase II	13	15	7	14	12	16	10	9	15	8	61	58
Phase III	8	7	8	6	4	7	9	7	9	5	33	37
Marketed	15	10	13	15	16	17	11	12	7	10	69	57
Total	51	39	40	42	40	49	44	44	44	31	212	212

Upfront Amounts for Acquisitions >$10M	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Preclinical	$1,831	$126	$686	$120	$124	$387	$523	$1,223	$941	$886	$2,887	$3,959
Phase I	$359	$66	$370	$368	$449	$1,026	$972	$690	$338	$762	$1,613	$3,788
Phase II	$1,384	$2,736	$1,294	$13,338	$4,445	$2,498	$2,596	$2,430	$9,328	$2,765	$23,197	$19,617
Phase III	$2,629	$1,993	$3,427	$1,425	$1,609	$2,272	$5,888	$22,372	$2,715	$13,228	$11,083	$46,476
Marketed	$19,680	$9,630	$11,598	$3,396	$16,390	$25,096	$19,285	$35,887	$22,165	$13,625	$60,693	$116,059
Total	$25,883	$14,553	$17,375	$18,646	$23,017	$31,278	$29,265	$62,603	$35,486	$31,266	$99,473	$189,898

Total Potential Amounts for Acquisitions >$10M	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Preclinical	$1,831	$126	$783	$488	$287	$1,222	$1,559	$2,063	$1,474	$4,178	$3,516	$10,496
Phase I	$541	$91	$1,194	$368	$1,507	$1,360	$2,328	$2,273	$1,425	$1,827	$3,700	$9,213
Phase II	$1,824	$4,493	$1,413	$14,834	$5,485	$4,123	$3,587	$7,840	$18,227	$3,654	$28,048	$37,432
Phase III	$2,849	$2,926	$4,988	$2,179	$4,184	$3,268	$7,038	$23,137	$3,028	$13,228	$17,127	$49,699
Marketed	$19,704	$10,223	$11,598	$4,125	$17,064	$25,350	$20,500	$37,025	$22,200	$13,917	$62,715	$118,992
Total	$26,750	$17,859	$19,977	$21,993	$28,526	$35,323	$35,012	$72,338	$46,354	$36,805	$115,105	$225,832

Table 9. Top: Number of acquisitions for global emerging therapeutic companies, by phase, 2008-2017. Center: Acquisition upfront amounts for global emerging therapeutic companies, by phase. Bottom: The number of acquisitions (with values above $10M) and total dollars raised per year for R&D-stage and market-stage companies.

Global R&D-Stage ETC Acquisitions by Disease

The number of R&D-stage acquisitions of oncology companies valued at >$10 million USD dropped form a record high of 13 in 2016 down to only 4 in 2017. That number includes the $11.9 billion acquisition of Kite Pharma that occurred just months before the FDA approval of Kite's CAR-T therapy, Yescarta, for Diffuse Large B-Cell Lymphoma (DLBCL). The Phase II oncology company Ignyta was purchased for $1.7 billion. The remaining two acquisitions were early stage (Preclinical and Phase I) and had most of the acquisition value tied to milestone dependent contingent value rights.

The decrease in R&D-stage acquisitions continued outside of oncology, except for disease areas that include metabolic, immunology, hematology and cardiovascular disorders. However, for each category there were no more than four acquisitions with disclosed values above $10 million. The metabolic interests coincide with the growing demand for rare disease products by larger pharmaceutical companies. The immunology demand was driven by lead products in autoimmune disorders that could have later crossover applications in immune-oncology. All three immunology acquisitions contained substantial contingent value rights tied to regulatory milestones.

GLOBAL AQUISITIONS OF R&D-STAGE THERAPEUTICS BY DISEASE, 2016 VS. 2017

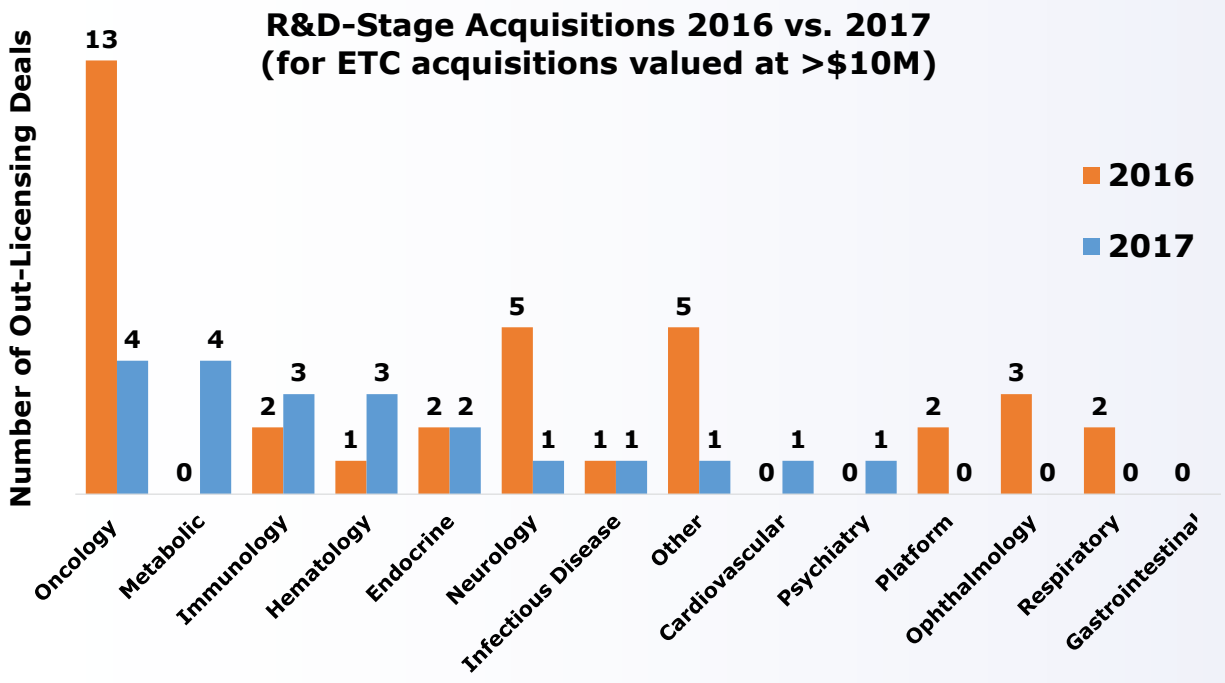


Chart 12. R&D-Stage Acquisitions in 2016 vs. 2017, by Disease Area, for deals with disclosed value above $10M. Acquisitions are sorted highest to lowest by number of deals in 2017.

ANNUAL GLOBAL AQUISITIONS OF R&D-STAGE THERAPEUTICS BY DISEASE, 2008-2017

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	9	8	4	11	7	10	12	5	13	4	39	44
Neurology	3	4	2	3	3	1	5	4	5	1	15	16
Infectious Disease	5	6	0	2	3	7	4	1	1	1	16	14
Endocrine	0	0	3	1	1	3	3	2	2	2	5	12
Platform	7	1	8	1	3	2	3	5	2	0	20	12
Metabolic	1	0	1	1	1	3	1	3	0	4	4	11
Immunology	3	2	1	2	1	0	1	2	2	3	9	8
Ophthalmology	0	3	0	0	0	1	2	2	3	0	3	8
Other	5	2	1	3	1	0	0	1	5	1	12	7
Cardiovascular	2	2	1	1	1	2	1	2	0	1	7	6
Respiratory	0	0	3	1	2	2	0	2	2	0	6	6
Hematology	1	1	0	0	1	1	0	0	1	3	3	5
Psychiatry	0	0	1	0	0	0	0	2	0	1	1	3
Gastrointestinal	0	0	2	1	0	0	1	1	0	0	3	2
Total	36	29	27	27	24	32	33	32	36	21	143	154

Disease Area	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology	$726	$1,773	$2,833	$2,218	$2,175	$2,616	$1,435	$1,011	$8,931	$13,922	$9,726	$27,914
Metabolic	$30	$0	$22	$610	$293	$74	$89	$8,716	$0	$536	$955	$9,415
Gastrointestinal	$0	$0	$390	$21	$0	$0	$1,027	$7,332	$0	$0	$411	$8,359
Infectious Disease	$916	$1,187	$0	$11,412	$2,131	$1,339	$5,827	$190	$0	$13	$15,646	$7,369
Neurology	$81	$703	$695	$210	$46	$37	$952	$3,644	$1,322	$1,027	$1,736	$6,982
Endocrine	$0	$0	$472	$71	$315	$730	$107	$2,722	$594	$180	$858	$4,333
Other	$1,553	$302	$70	$175	$9	$0	$0	$229	$815	$534	$2,109	$1,578
Immunology	$1,012	$221	$102	$186	$1,272	$0	$260	$330	$275	$620	$2,793	$1,485
Hematology	$400	$255	$0	$0	$94	$240	$0	$0	$665	$571	$749	$1,476
Respiratory	$0	$0	$204	$328	$178	$600	$0	$260	$500	$0	$710	$1,360
Cardiovascular	$538	$153	$165	$10	$3	$336	$42	$600	$0	$137	$868	$1,114
Ophthalmology	$0	$298	$0	$0	$0	$160	$67	$679	$170	$0	$298	$1,075
Platform	$946	$29	$598	$10	$111	$51	$175	$541	$50	$0	$1,695	$817
Psychiatry	$0	$0	$226	$0	$0	$0	$0	$462	$0	$100	$226	$562
Total	$6,203	$4,923	$5,777	$15,250	$6,627	$6,182	$9,979	$26,716	$13,321	$17,640	$38,780	$73,839

Table 10. R&D-stage acquisitions, 2008-2017. 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.

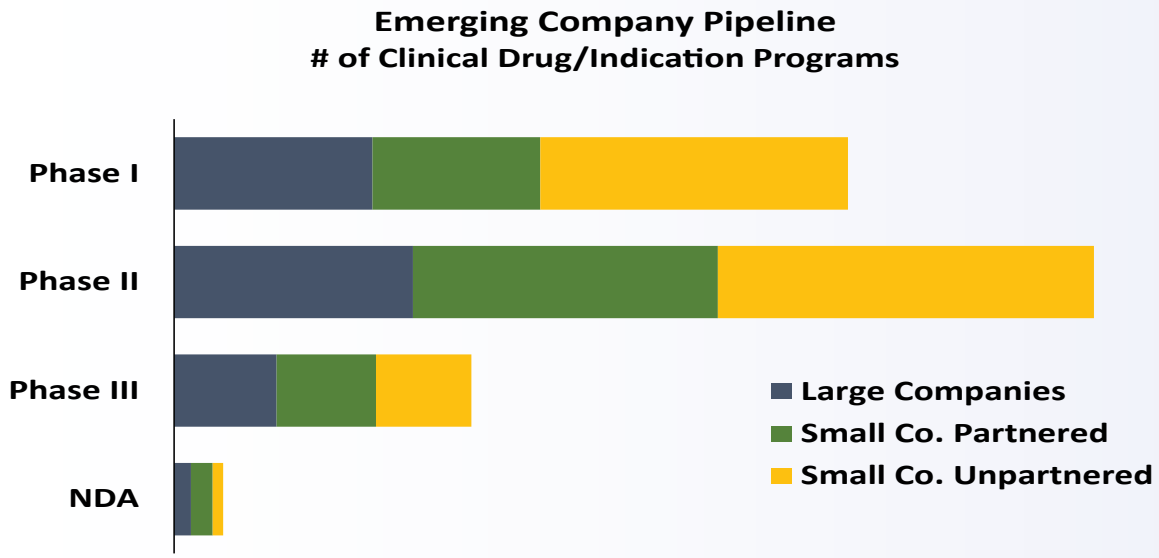
Clinical Pipeline for Emerging Companies

Emerging companies have a robust pipeline, with 4,763 drug indication programs under development, either independently or partnered. This accounts for 71% of the entire global industry pipeline, which stands at 6,679 programs.

Roughly 43% of emerging company programs are partnered with other companies, demonstrating the importance of licensing and collaborations in the biopharmaceutical industry. Almost half of the emerging therapeutic company pipeline is in Phase II (48%). Only 14% of emerging therapeutic company programs are in Phase III, 51% of which are partnered. Of the 169 total industry NDA/BLAs submitted as of March 2018, 111 (66%) involved an emerging company.

For each disease area analyzed in **Table 11**, emerging therapeutic company programs (partnered or unpartnered) outnumber programs among the large biopharmaceutical companies. Oncology makes up the largest percentage of the emerging company clinical pipeline (39%) and has the highest percentage of partnered programs (50%). Cardiovascular and Psychiatry have the lowest percentage of partnered programs (35% and 33%, respectively).

EMERGING COMPANY CLINICAL-STAGE PIPELINE



# of Clinical Programs	Phase I	Phase II	Phase III	NDA	Total	% of Total
Small Co. Unpartnered	1059	1295	328	36	2718	40.7%
Small Co. Partnered	578	1050	342	75	2045	30.6%
Large Companies	683	822	353	58	1916	28.7%
Total	2320	3167	1023	169	6679	100%

Chart 13. Number of clinical Drug/Indication programs (Phase I, II, III, and NDA/BLA-stage) in the pipeline at emerging therapeutic companies (blue partnered, light blue unpartnered) and large biopharmaceutical developers (dark blue, includes Large to Large company partnered programs). Based on analysis of the BioMedTracker database accessed March 2018.

CLINICAL PIPELINE BY DISEASE AREA AND COMPANY SIZE

Disease	Type	P1	P2	P3	NDA/BLA	Total
Oncology	ETC Unpartnered	445	413	74	2	934
	ETC Partnered	330	480	108	14	932
	Large Companies	341	357	103	12	813
Neurology	ETC Unpartnered	151	166	51	10	378
	ETC Partnered	54	101	44	9	208
	Large Companies	48	60	46	4	158
Infectious Disease	ETC Unpartnered	117	105	29	4	255
	ETC Partnered	38	63	26	12	139
	Large Companies	44	56	31	4	135
Immunology	ETC Unpartnered	54	102	24	1	181
	ETC Partnered	34	65	27	4	130
	Large Companies	54	82	45	14	195
Other	ETC Unpartnered	53	120	35	2	210
	ETC Partnered	25	77	35	7	144
	Large Companies	60	47	22	4	133
Endocrine	ETC Unpartnered	63	84	22	4	173
	ETC Partnered	13	58	15	6	92
	Large Companies	36	35	23	2	96
Cardiovascular	ETC Unpartnered	38	65	19	2	124
	ETC Partnered	9	31	18	2	60
	Large Companies	17	24	11	6	58
Ophthalmology	ETC Unpartnered	19	65	18	4	106
	ETC Partnered	9	48	13	2	72
	Large Companies	13	33	14	1	61
Respiratory	ETC Unpartnered	31	38	5	0	74
	ETC Partnered	18	41	9	2	70
	Large Companies	21	47	18	1	87
Metabolic	ETC Unpartnered	23	42	14	2	81
	ETC Partnered	13	26	17	4	60
	Large Companies	15	20	7	2	44
Gastroinstential	ETC Unpartnered	24	38	9	0	71
	ETC Partnered	18	26	11	3	58
	Large Companies	14	26	9	3	52
Hematology	ETC Unpartnered	22	26	12	2	62
	ETC Partnered	7	19	13	8	47
	Large Companies	7	16	14	4	41
Psychiatry	ETC Unpartnered	19	31	16	3	69
	ETC Partnered	10	15	6	2	33
	Large Companies	13	19	10	1	43
	Total	2320	3167	1023	169	6679

Table 11. Number of clinical programs by disease area for emerging therapeutic company (ETC, partnered vs. unpartnered), and large biopharmaceutical companies as of March 2018.

Rare Disease

According to a recent report from Global Genes, there are 7,000 rare diseases that cumulatively affect 30 million Americans.[1] Approximately 350 therapeutics are approved for these diseases, indicating that thousands of rare diseases are without a treatment or cure.

Venture Capital: Over the last ten years, there has been an increase in investment into rare diseases (ex-oncology), with the highest amount seen in 2017 ($1.3 billion).

ANNUAL US VENTURE FUNDING OF RARE DISEASES, 2008-2017
AND ORPHAN DRUG PIPELINE FOR EMERGING THERAPEUTIC COMPANIES

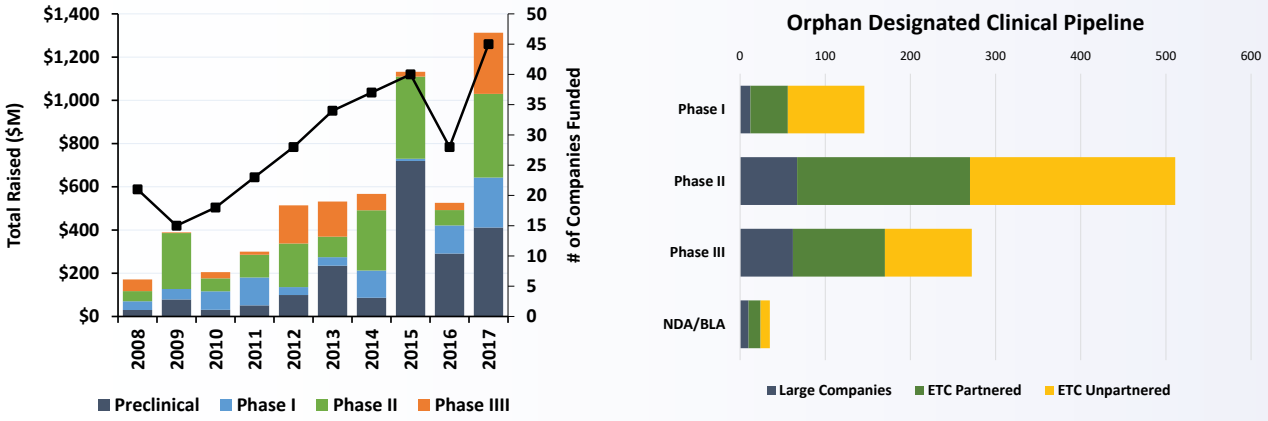


Chart 14. Left: Annual venture funding ($M) into companies with a lead drug in a rare disease (ex-oncology), 2008-2017. Investments are displayed by R&D Phase and the number of companies receiving financing per year for a specific venture round are displayed as a line. Right: Clinical pipeline for all Orphan Designated products (including rare cancers) developed by emerging companies and large companies as of March 2018.

IPOs: The number of rare disease IPOs was up from just three in 2016 to eight in 2017, the second highest number in a decade.

Licensing and Acquisitions: For most of the decade (2008-2014), the number of licensing transactions (>$10M potential value) for rare diseases has been greater than 10 each year. From 2015-2017 this has decreased to below 10 each year, with 2017 recording nine licensing deals. Acquisitions of rare disease companies (ex-oncology) jumped from three in 2016 to seven in 2017.

Pipeline: The number of Orphan programs increased from 806 in 2017 to 964 in 2018. Programs for the treatment of rare cancer account for 394 of these Orphan programs. Small emerging companies account for 84% of all Orphan-designated products in clinical development as shown in **Chart 14**.[2]

1 http://globalgenes.org/rare-diseases-facts-statistics
2 Orphan-designation as described under the Orphan Drug Act of 1983 (Public Law 97-414)

Discussion

The aim of this study was to accurately define the levels of funding and deal interest in small drug development 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.

Overall, across both investments and deal-making, there continues to be an emphasis on oncology and rare diseases over high prevalence disease areas such as cardiovascular and psychiatry. For example, venture investment into novel drug R&D has declined for companies focused on psychiatry, cardiovascular, endocrine, respiratory, gastrointestinal diseases. To investigate these areas more broadly, BIO has launched a series of reports that focus on the state of innovation in a specific chronic indication. Reports on Depression, Pain and Addiction can be found at www.bio.org/iareports.

Although dollar amounts invested in the smallest start-ups reached an all-time high for Series A financings, we continue to see a ceiling of less than 90 companies raising their first Series A round. As this is a proxy for first sizable VC-backed funding of a company, it begs the question if entrepreneurs working on highly prevalent chronic diseases are receiving the same opportunities to innovate as the oncology and rare disease start-ups.

The public markets remain healthy for small emerging companies looking to raise funds either through IPOs or through follow-on offerings

Healthy R&D-stage licensing deal activity returned in 2017 from the small decline observed in 2016. A total of 139 deals with disclosed values above $10 million brought in $4.4 billion into small biotechs through licensing upfront payments. With 2,718 emerging company programs unpartnered as of March 2018, there remains a substantial number of opportunities for larger biopharmaceuticals companies.

The number of acquisitions of R&D-stage companies in 2017 was unusually low (21). More than half of the dollars spent on R&D-stage acquisitions went to a single CAR-T company, Kite Pharma. Rare disease companies saw a surge in acquisitions from 2016 levels. With respect to acquisitions of market-stage emerging companies, 2017 saw 10 companies acquired for more than $13 billion. Companies successful with product-launches remain strategically attractive as bolt-on additions to large company franchises.

At a higher level, we see recent acquisition activity targeted at market-stage and Phase III companies, and licensing more focused upstream at the Preclinical stage. Within venture capital, the strength is seen in Preclinical-stage companies, while IPOs were typically at Phase II and FOPOs strongest with Phase III companies. This is indicative of the roles various capital inputs have along the drug development path, but the variance seen within certain disease areas demands close monitoring in the coming years.

Maintaining balance through funding cycles can be challenging but manageable with a sound policy environment. It is imperative that the right policy environment is maintained to ensure that biopharmaceutical companies can develop new medicines and solutions that address our most pressing and emerging public health needs. Over the period of this study, a number of policies have buttressed the industry through difficult and uncertain times. Notable examples such as the JOBS Act, FDASIA (including PDUFA V), FDARA (PDUFA VI), 21st Century Cures, the Biologics Price Competition and Innovation Act (12 years of data exclusivity for biologics), the R&D Tax Credit, and the Orphan Drug Tax Credit have helped strengthen a diverse innovation ecosystem. With respect to the Orphan Drug Tax Credit, we will be monitoring the effects of the recently enacted US tax reform law that cut this vital benefit in half.

Continued investment requires strong intellectual property protections, a regulatory system that is reflective of current and emerging medical science, incentives for private and public-sector investment in this innovative industry, and a biopharmaceutical marketplace that appropriately values and rewards such high-risk investment.

Methodology

Definitions:

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.

Data Sources

Venture Capital: 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. 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 2008 to 2017 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 diseases and by sub-indication – these indications are listed in the Appendix.

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, and FierceBiotech. Disease areas and phase were tagged according to lead product in R&D at the time of investment.

FOPOs: 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: Primary data sources on acquisitions were Informa Strategic Transactions, Recap (Thomson Reuters), 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.

Appendix

Disease-Subindication	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Oncology - Oncology	$1,136	$919	$616	$923	$740	$1,042	$1,225	$2,053	$1,567	$2,918	$4,333	$8,805
CV - Hypercholesterolemia	$12	$2	$13	$51	$16	$54	$0	$118	$0	$40	$94	$212
CV - Hypertension	$10	$11	$25	$3	$10	$13	$1	$1	$0	$13	$59	$28
CV - Other Indication	$191	$115	$93	$202	$257	$109	$55	$126	$51	$74	$859	$416
CV - Multiple Indications	$8	$39	$10	$0	$0	$0	$0	$0	$0	$0	$56	$0
ID - Antimicrobial g+	$31	$134	$50	$74	$70	$65	$101	$19	$60	$1	$359	$246
ID - Antimicrobial g-	$46	$2	$5	$44	$9	$70	$10	$41	$76	$153	$105	$350
ID - Antimicrobial broad	$73	$19	$114	$65	$0	$28	$147	$117	$112	$56	$270	$459
ID - Anti-fungal	$39	$75	$6	$22	$3	$41	$102	$135	$9	$67	$146	$353
ID - Antiviral - other	$25	$95	$20	$71	$14	$55	$99	$84	$38	$628	$225	$905
ID - HCV	$89	$43	$25	$12	$0	$21	$13	$0	$0	$0	$169	$34
ID - HIV	$50	$16	$18	$42	$15	$11	$0	$15	$0	$10	$142	$36
ID - Vaccine	$82	$63	$84	$53	$56	$59	$36	$163	$486	$44	$338	$789
ID - Other Indication	$0	$6	$1	$0	$0	$0	$27	$0	$0	$1	$7	$28
ID - Multiple Indications	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Immunology - Arthritis	$86	$5	$29	$8	$56	$0	$109	$5	$116	$23	$183	$252
Immunology - Psoriasis	$6	$2	$2	$0	$11	$10	$74	$18	$0	$31	$21	$133
Immunology - Other Indication	$122	$106	$83	$49	$70	$116	$79	$187	$171	$116	$430	$669
Immunology - Multiple Indications	$97	$44	$38	$0	$11	$45	$0	$48	$45	$25	$190	$162
Endocrine - T2D	$138	$23	$37	$180	$219	$29	$229	$207	$517	$427	$597	$1,409
Endocrine - T1D	$5	$16	$8	$3	$0	$14	$3	$33	$11	$81	$31	$142
Endocrine - Other Indication	$66	$138	$32	$96	$65	$114	$74	$132	$360	$165	$397	$845
Endocrine - Multiple Indications	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Metabolic - Obesity	$37	$11	$32	$73	$21	$35	$12	$43	$3	$44	$173	$137
Metabolic - Genetic Disorder	$29	$100	$31	$133	$235	$97	$135	$343	$162	$335	$527	$1,072
Metabolic - Other Indication	$19	$51	$113	$35	$115	$133	$14	$12	$8	$0	$334	$168
Metabolic - Multiple Indications	$8	$0	$0	$0	$0	$0	$0	$24	$2	$0	$8	$26
Psychiatry - Schizophrenia	$0	$2	$0	$0	$19	$18	$17	$0	$0	$0	$21	$35
Psychiatry - Depression	$36	$4	$38	$27	$75	$7	$121	$4	$0	$14	$180	$146
Psychiatry - Other Indication	$0	$44	$0	$31	$17	$19	$16	$36	$13	$21	$92	$105

A1. Venture capital, by sub-indication ($M invested per year), 2008-2017.

Appendix

Disease-Subindication	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	5 yr period 2008-2012	5 yr period 2013-2017
Psychiatry - Multiple Indications	$0	$0	$0	$0	$0	$0	$0	$0	$40	$0	$0	$40
Neurology - Pain	$158	$245	$124	$106	$161	$97	$137	$159	$41	$171	$793	$605
Neurology - Parkinson's	$0	$0	$26	$10	$15	$39	$117	$196	$10	$36	$51	$397
Neurology - Alzheimer's	$44	$47	$48	$31	$34	$54	$28	$145	$289	$84	$204	$600
Neurology - MS	$129	$40	$2	$9	$17	$21	$5	$0	$0	$0	$196	$26
Neurology - Other Indication	$31	$181	$66	$21	$78	$134	$169	$282	$275	$524	$376	$1,384
Neurology - Multiple Indications	$91	$19	$50	$8	$18	$30	$0	$217	$22	$35	$185	$304
Respiratory - Asthma	$39	$52	$31	$9	$3	$6	$38	$4	$0	$0	$133	$48
Respiratory - COPD	$20	$0	$59	$49	$53	$42	$0	$0	$8	$5	$181	$55
Respiratory - Other Indication	$106	$22	$65	$34	$6	$13	$21	$206	$130	$164	$233	$533
Respiratory - Multiple Indications	$4	$32	$0	$14	$3	$0	$0	$0	$0	$0	$53	$0
Hematology - Blood Stimulator	$3	$3	$22	$52	$63	$3	$0	$0	$26	$0	$143	$29
Hematology - Coagulation	$40	$25	$22	$0	$7	$11	$32	$93	$4	$48	$95	$188
Hematology - Other Indication	$65	$56	$60	$39	$80	$77	$10	$69	$36	$0	$300	$192
Hematology - Multiple Indications	$0	$6	$0	$0	$0	$0	$0	$0	$0	$0	$6	$0
GI - IBS	$85	$39	$18	$30	$30	$26	$11	$18	$8	$83	$202	$144
GI - GERD	$5	$0	$0	$0	$0	$0	$0	$0	$0	$0	$5	$0
GI - Crohn's	$105	$0	$0	$0	$16	$0	$0	$38	$0	$0	$121	$38
GI - Ulcerative Colitis	$6	$0	$0	$0	$19	$1	$2	$0	$0	$29	$25	$32
GI - Other Indication	$6	$0	$49	$35	$22	$26	$5	$0	$8	$4	$113	$42
GI - Multiple Indications	$0	$0	$0	$1	$0	$0	$0	$20	$3	$0	$1	$23
Ophthalmology	$138	$196	$92	$216	$107	$275	$272	$166	$231	$215	$748	$1,159
PLATFORM	$180	$221	$250	$141	$286	$341	$874	$1,015	$428	$454	$1,077	$3,113
Other - Allergy	$0	$0	$0	$0	$0	$29	$41	$93	$10	$269	$0	$442
Other - Dermatology	$49	$62	$81	$80	$72	$110	$120	$155	$66	$57	$344	$508
Other - Renal	$67	$53	$71	$27	$103	$45	$70	$81	$82	$111	$322	$390
Other - Chemo/Rad side effects	$0	$10	$20	$44	$58	$0	$0	$0	$0	$0	$134	$0
Other - Other Indication	$57	$47	$84	$35	$134	$53	$101	$84	$74	$154	$357	$465
Other - Multiple Indications	$97	$53	$64	$19	$0	$46	$0	$16	$40	$62	$232	$164

A1. Venture capital, by sub-indication ($M invested per year), 2008-2017.

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