



# Emerging Therapeutic Company Investment and Deal Trends

US Venture Capital and Public Offerings, 2006-2015  
Global Licensing and Acquisitions, 2006-2015  
Current Pipeline for Emerging Companies

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by **David Thomas, CFA** and **Chad Wessel**  
**BIO INDUSTRY ANALYSIS**



Biotechnology  
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## 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.

# Letter from the Honorable Jim Greenwood & Dr. Cartier Esham

May 25, 2016

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 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 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:** 2015 was the best year on record for US venture capital, with just under \$7 billion raised. Funding of immuno-oncology and neurodegenerative disease companies helped drive this all-time high. Investment in treatments for neurological diseases continued to rise. However, a few disease areas affecting large populations (endocrine, respiratory and gastrointestinal) continues to see declines in recent years.
- **Series A Financing:** Series A financing nearly doubled from 2014 to 2015. The number of first-time Series A investments reached 80 for the first time in nine years.
- **IPOs:** The IPO market continued to be strong since the passage of the JOBS Act in 2012. In 2015, 39 US emerging therapeutic companies listed on public exchanges.
- **Follow-On Public Offerings:** FOPOs by US emerging companies set a record high in 2015, with \$16.1 billion raised.
- **Licensing:** 2015 saw an all-time high of \$7.1 billion for upfront payments in R&D-stage licensing deals.
- **Acquisitions:** Acquisitions of R&D-stage companies in 2015 raised \$26.3 billion in upfront payments, a record high.

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*



# Table of Contents

## Trends by Phase of Development and Disease Area

Introduction .....	6
Venture Capital .....	10
IPOs .....	18
Follow-on Offerings.....	20
Licensing .....	22
Acquisitions .....	27
Clinical Pipeline .....	30
Rare Disease.....	32
Discussion .....	33
Methodology.....	34
Appendix.....	36



# Emerging Therapeutic Company Investment and Deal Trends by Phase of Development, 2006-2015

## 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 analyzed the most recent 10 years of data in these core areas using six databases to create the broadest, most comprehensive study possible. The Thomson Reuters Cortellis Venture Intelligence and ReCap products, Informa's Strategic Transactions and BioMedtracker Databases, BioCentury's BCIQ, and EvaluatePharma were indispensable resources for this endeavor.

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 snapshots are provided to give context on the degree of industry partnering and contribution of emerging companies. This broad-based analysis will help identify where scientific or policy issues may be impacting the ability to maintain a robust emerging company pipeline of innovative medicines – a goal that is shared by patients, healthcare providers, policymakers, investors, and the biopharmaceutical industry alike.

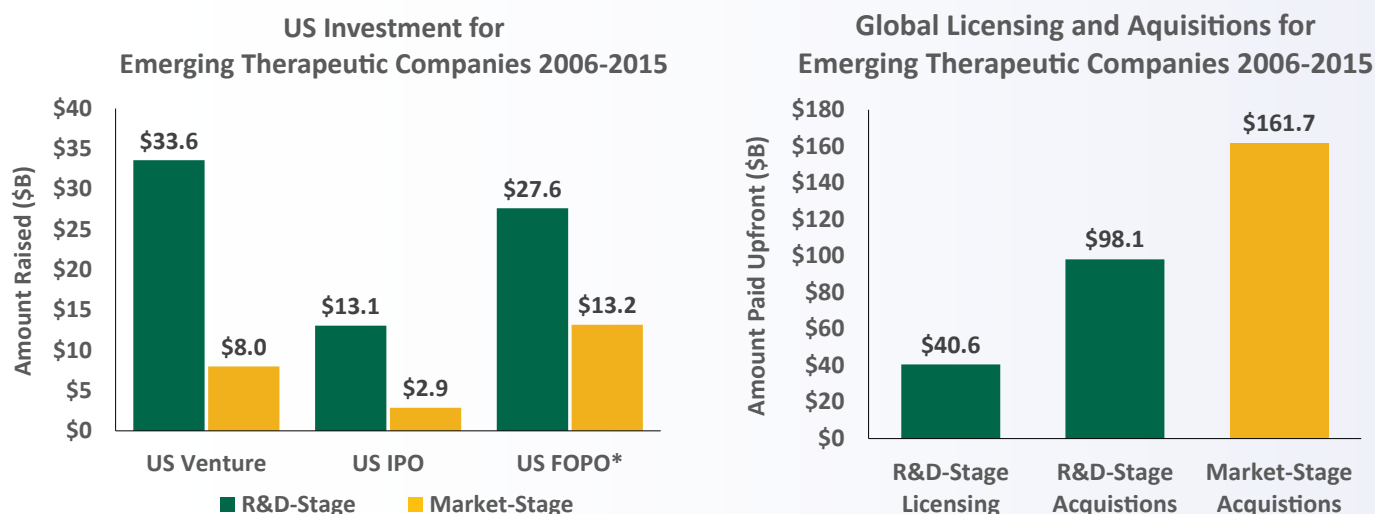
Private emerging companies working on innovative therapeutics are highly dependent on access to capital. For early-stage private companies, the majority of this investment funding comes in the form of venture capital until the eventual listing on a public exchange. This initial public offering is the first of what can be many rounds of financing from public investors. All three of these events – venture financing, IPOs, and FOPOs – are impactful for emerging companies, and are captured in this report by both stage of clinical development and lead therapeutic category 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 acquisitions aims to shed light on where the disease focus has been for global drug developers seeking to add innovation from emerging companies into their own pipeline or portfolio of products. For both licensing and acquisitions, emerging company transactions are presented in this report globally.

## 2006-2015 Emerging Company Investment and Deal Making

Over the last decade, a total of \$98.4 billion in investment dollars went into US emerging therapeutic companies through venture capital (42%), follow-on public offerings (41%), and initial public offerings (16%). More than \$138 billion went into upfront payments for either in-licensing assets from (30%) or acquiring (70%) global R&D-stage emerging companies. Although there were far fewer total acquisition transactions than licensing transactions (by an order of magnitude), larger biopharma companies spent \$161.7 billion over the last 10 years on market-stage acquisitions.

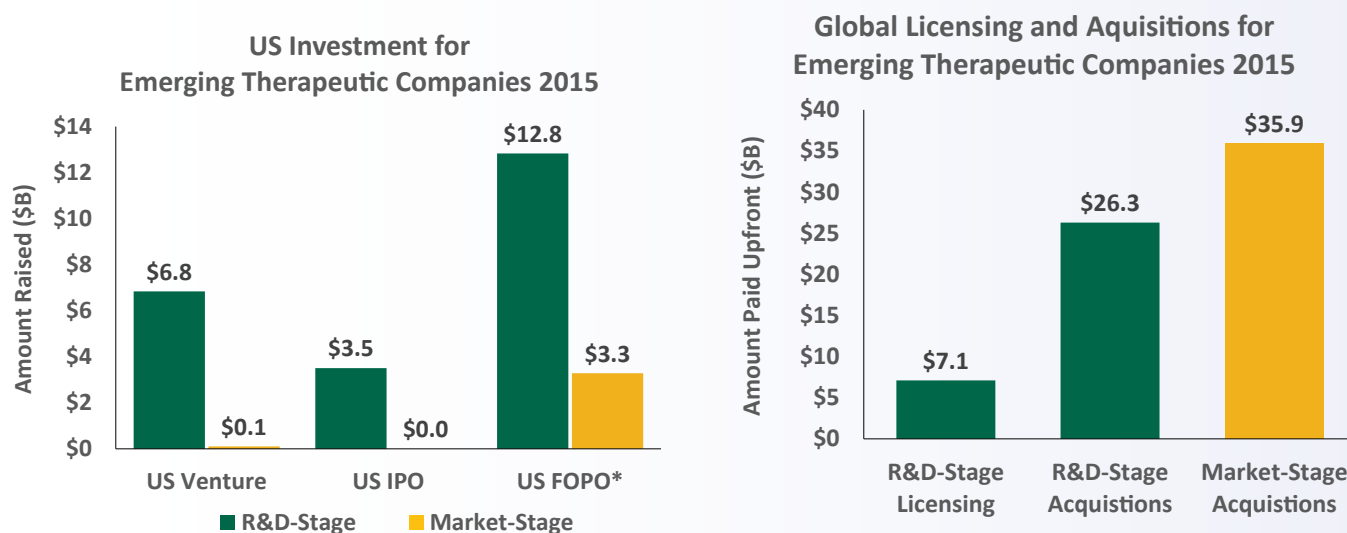
## TOTAL EMERGING THERAPEUTICS INVESTMENT AND DEAL-MAKING, 2006-2015



**Chart 1. Left: Breakdown of emerging company investment in the US from 2006-2015. Right: Breakdown of large company spending (as upfront payments) to access innovation through licensing deals and acquisitions with global emerging biotech companies.**

A similar breakdown for the year 2015 shows some differences in the percentage allocation of the US investment in emerging therapeutic companies, which totaled \$26.5 billion. For example, more money was raised in FOPOs than venture capital, and hardly any investment went into market-stage venture deals or IPOs.

## TOTAL EMERGING THERAPEUTICS INVESTMENT AND DEAL-MAKING, 2015



**Chart 2. Left: Breakdown of emerging company investment in the US in 2015. Right: Breakdown of large company spending (as upfront payments) to access innovation through licensing deals and acquisitions with emerging biotech companies.**

## US Investment by Disease, 2006-2015

US Investment (\$M) 2006-2015	US Venture		US IPO		US FOPO		Total	
Oncology	\$10,357	27%	\$3,607	28%	\$14,549	36%	\$28,514	26%
Infectious Disease	\$4,163	11%	\$1,582	12%	\$8,398	21%	\$14,143	13%
Neurology	\$4,239	11%	\$2,203	17%	\$6,298	15%	\$12,739	12%
Metabolic	\$2,439	6%	\$854	7%	\$6,391	16%	\$9,683	9%
Endocrine	\$2,488	6%	\$919	7%	\$4,672	11%	\$8,079	7%
Other Diseases	\$2,890	8%	\$1,766	14%	\$2,465	6%	\$7,120	6%
Immunology	\$1,857	5%	\$622	5%	\$2,705	7%	\$5,184	5%
Cardiovascular	\$2,182	6%	\$643	5%	\$2,161	5%	\$4,986	5%
Hematology	\$1,112	3%	\$1,777	14%	\$1,678	4%	\$4,567	4%
Platform	\$3,931	10%	\$217	2%	\$0	0%	\$4,148	4%
Ophthalmology	\$1,913	5%	\$774	6%	\$1,152	3%	\$3,839	3%
Gastrointestinal	\$956	2%	\$557	4%	\$1,772	4%	\$3,285	3%
Respiratory	\$1,219	3%	\$218	2%	\$1,157	3%	\$2,594	2%
Psychiatry	\$687	2%	\$190	1%	\$174	0%	\$1,051	1%
<b>Total</b>	<b>\$40,432</b>	<b>100%</b>	<b>\$15,928</b>	<b>100%</b>	<b>\$53,572</b>	<b>100%</b>	<b>\$109,932</b>	<b>100%</b>

**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 includes 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.**



## Global Deals by Disease, 2006-2015

Global Deals (\$M) 2006-2015	Licensing R&D-Stage		Acquisitions R&D-Stage		Acquisitions Market-Stage		Total	
Oncology	\$11,478	32%	\$20,900	27%	\$55,945	40%	\$88,323	29%
Other Diseases	\$2,458	7%	\$2,883	4%	\$36,890	27%	\$42,232	14%
Infectious Disease	\$3,370	9%	\$24,821	32%	\$4,685	3%	\$32,877	11%
Immunology	\$2,793	8%	\$4,384	6%	\$20,231	15%	\$27,408	9%
Gastrointestinal	\$1,551	4%	\$9,101	12%	\$12,267	9%	\$22,919	8%
Endocrine	\$2,804	8%	\$5,055	7%	\$7,238	5%	\$15,097	5%
Respiratory	\$1,097	3%	\$1,570	2%	\$11,580	8%	\$14,247	5%
Neurology	\$4,653	13%	\$7,275	10%	\$2,317	2%	\$14,246	5%
Metabolic	\$1,925	5%	\$9,852	13%	\$960	1%	\$12,738	4%
Cardiovascular	\$2,030	6%	\$4,440	6%	\$3,888	3%	\$10,359	3%
Platform	\$2,995	8%	\$4,185	5%	\$0	0%	\$7,180	2%
Psychiatry	\$743	2%	\$717	0.9%	\$3,824	2.8%	\$5,284	2%
Ophthalmology	\$1,121	3%	\$1,952	3%	\$561	0%	\$3,635	1%
Hematology	\$1,356	4%	\$989	1%	\$1,282	1%	\$3,627	1%
<b>Total</b>	<b>\$40,377</b>	<b>100%</b>	<b>\$98,125</b>	<b>100%</b>	<b>\$161,669</b>	<b>100%</b>	<b>\$300,171</b>	<b>100%</b>

**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 of marketed products tend to be regional sales & marketing agreements with different characteristics than those of R&D-stage deal terms. Such deals have been excluded from this analysis, as they do not offer the best representation of large company pipeline interests nor 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. With respect to market-stage acquisitions, it should be noted that a number of companies that meet our definition of emerging company fall into the “Specialty Pharma” area with multiple products on the market and no standout lead product. They are thus grouped into the “Other” category.**

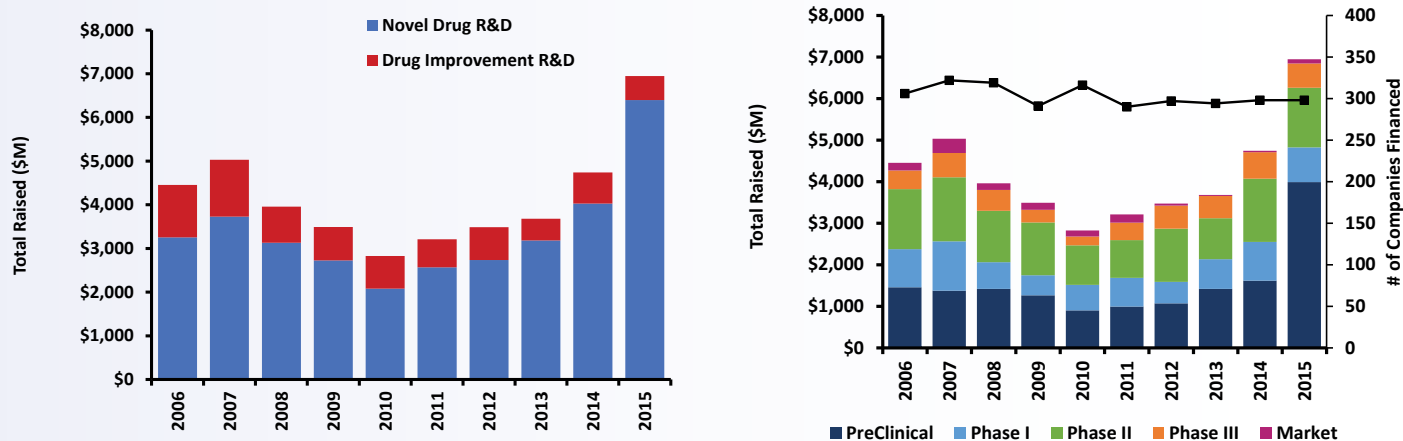
## Venture Capital Funding of US Therapeutic Companies

Venture capital investments are categorized according to level of novelty, as well as by phase of clinical development and disease area. 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.

As shown in **Chart 3**, venture equity funding of private drug development companies set a new record in 2015, with \$6.8 billion in total capital raised. Although 2014 was a strong year (\$4.7 billion), approaching the previous high water mark of 2007 (\$5 billion), 2015 surpassed these previous record years by nearly \$2 billion. This is in part due to seven companies receiving large investments of over \$100 million each, totaling more than \$1.3 billion. One of 2015’s significant deals was the largest VC investment in biotech history (\$446 million).

The majority (nearly 70%) of 2015 venture investment dollars went into early-stage companies with lead products in Preclinical or Phase I trials. Early-stage funding reached a decade high in 2015, due in large part to 22 companies raising over \$50 million apiece. These 22 companies alone made up nearly half of all early-stage investment in 2015.

### VENTURE FUNDING OF US THERAPEUTIC COMPANIES, 2006-2015



**Chart 3. Total venture funding from 2006-2015. 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 by Disease

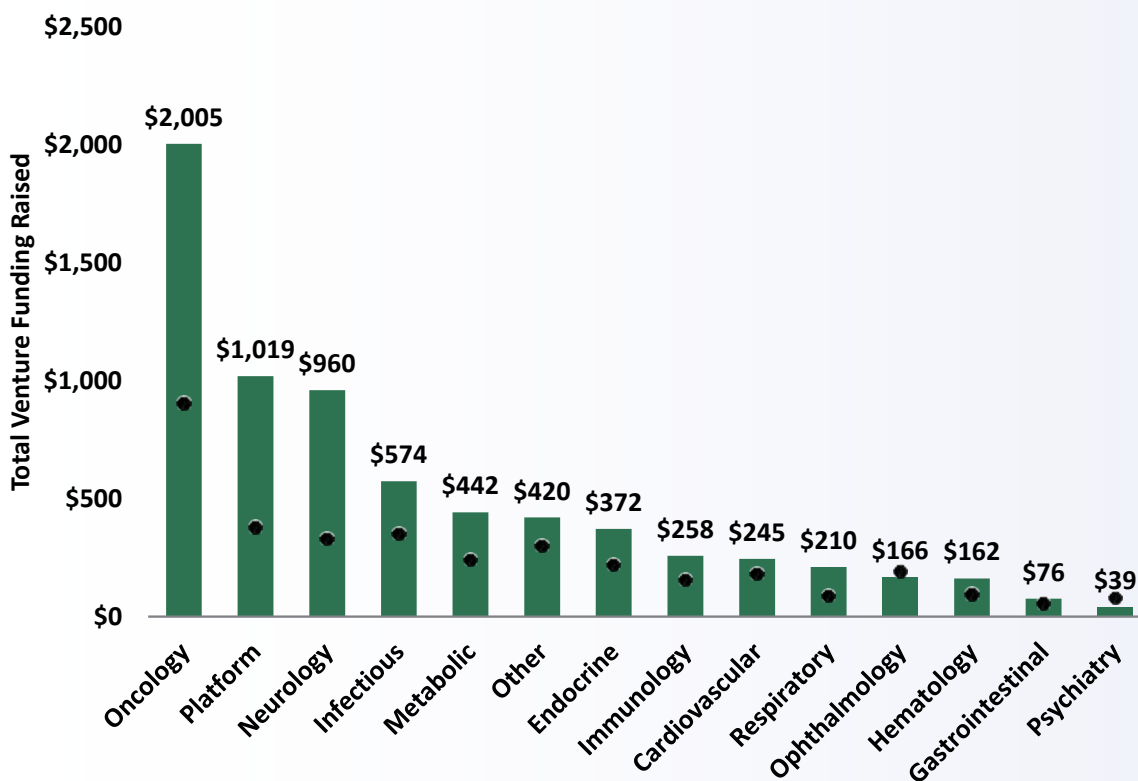
Over the past 10 years, US venture funding for oncology companies has consisted of nearly 30% of all venture funding. The majority of this (89%) went toward novel R&D investment. This trend continued in 2015, with the largest year seen for oncology companies in a decade (over \$2 billion in venture funding). This is 66% more than the \$1.2 billion invested in 2014. Surprisingly, this large increase in funding was not due to a few outlier rounds. Only two of the oncology companies out of the 80 that received funding in 2015 received over \$100 million.

For the fifth year in a row, neurology companies experienced an increase in venture investment. 2015 investment in neurology more than doubled from the amount invested in 2014 (\$960 million vs. \$456 million). Nearly 40% of those companies had lead products in either Alzheimer's or Parkinson's disease at the time of the investment.

Investment in metabolic disease saw a nearly 300% increase in investment in 2015 when compared to 2014. Out of the 16 transactions that took place in 2015, 11 were for companies that had lead products for rare genetic disorders, accounting for \$339 million out of the \$442 million invested.

Companies with lead programs in psychiatry and gastrointestinal diseases received the least amount of funding 2015, with \$39 million and \$76 million being invested respectively.

### VENTURE FUNDING OF US THERAPEUTIC COMPANIES BY DISEASE 2015 VS. 2010-2014 AVERAGE

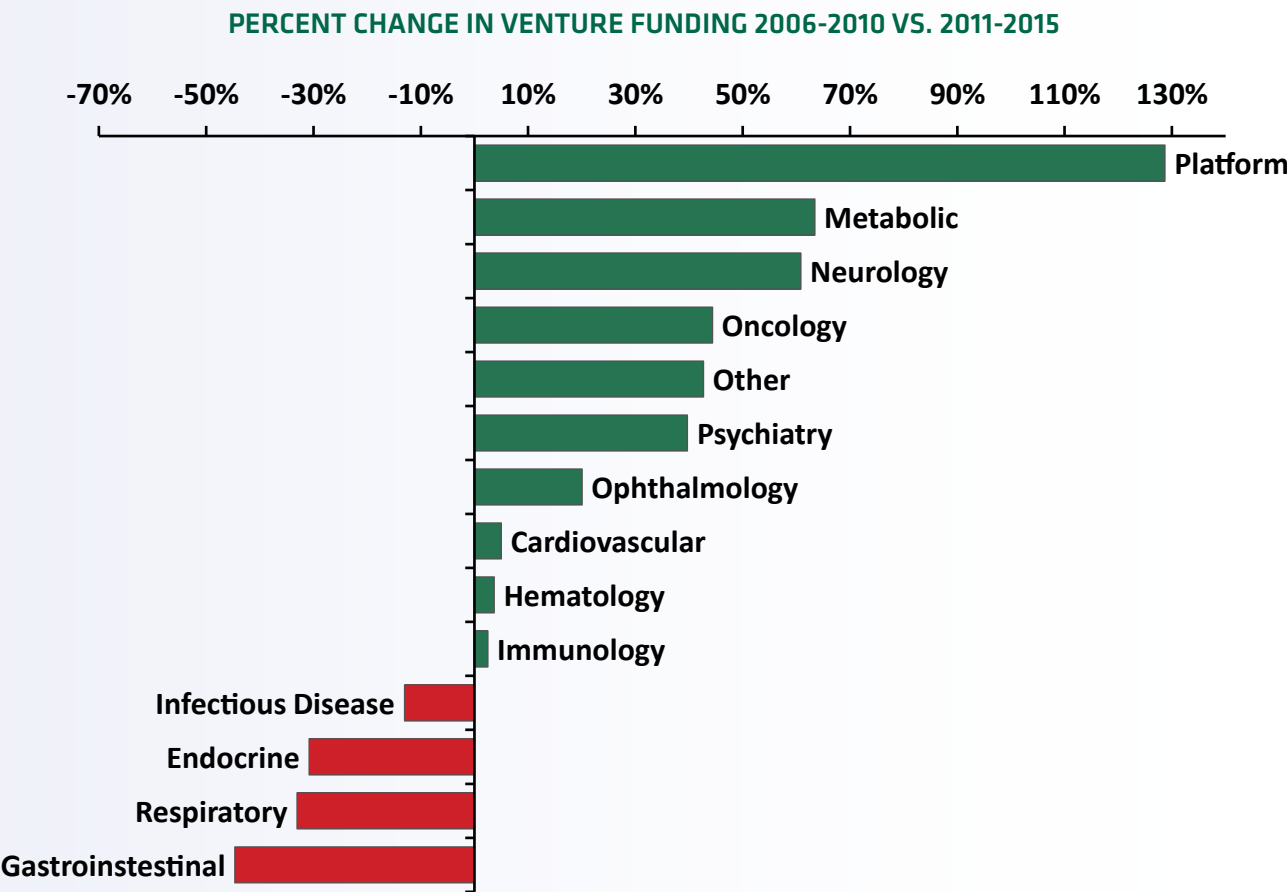


**Chart 4. Total venture funding in 2015, sorted highest to lowest funding by disease. Black dots represent the previous 5-year average (2010-2014).**

A look at novel R&D funding over the two five-year periods 2006-2010 vs. 2011-2015 (in **Chart 5**) reveals platform technology investment outpacing all other categories on a percentage change basis. In dollar terms, platform investment increased \$1.4 billion over the two five-year periods, the second largest after oncology's \$1.7 billion increase.

Metabolic and Neurology gains of >50% are largely due to an outstanding 2015, as explained above. This big year drove the most recent five-year period to increase more than \$500 million for both areas.

Four disease areas, each with high prevalence indications (gastrointestinal, respiratory, endocrine, and infectious disease), have seen decreases in funding over the two five-year periods. Previous iterations of this report found significant drops in high prevalence indications when comparing 2004-2008 vs. 2009-2013 and 2005-2009 vs. 2010-2014. As the first five year window begins to encompass the low investment periods impacted by the financial crisis (2008-2011), a recovery in venture investing should show more disease areas with positive changes.



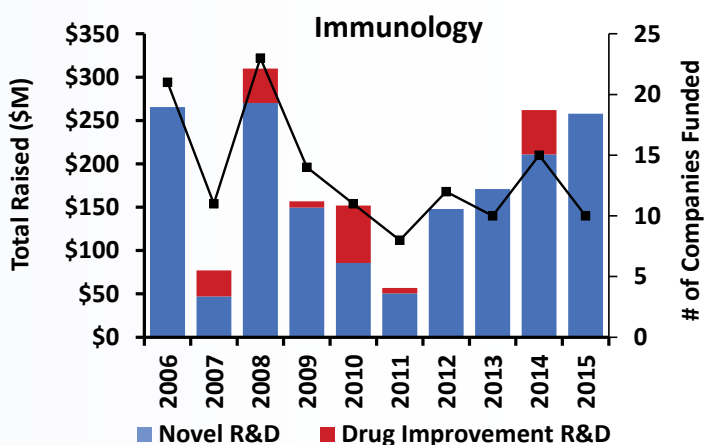
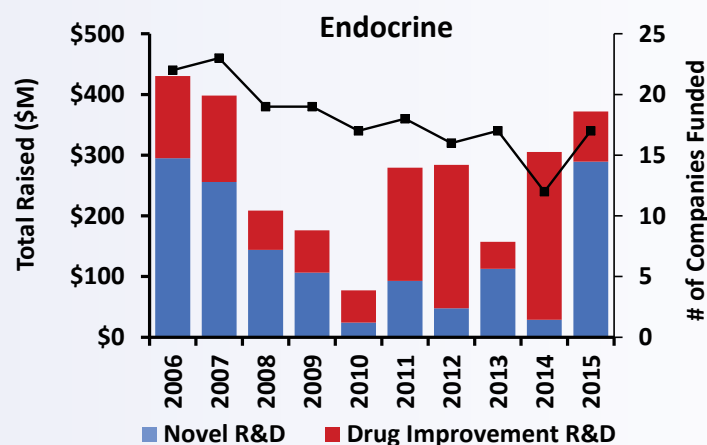
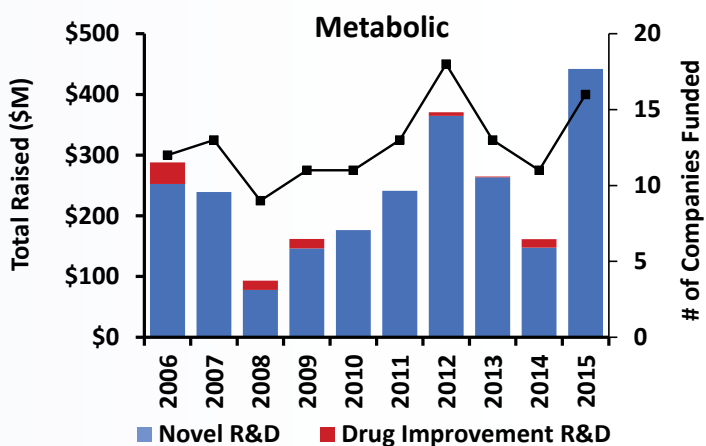
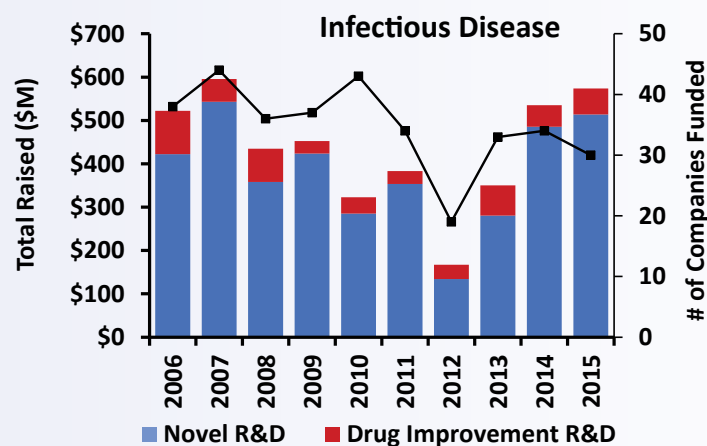
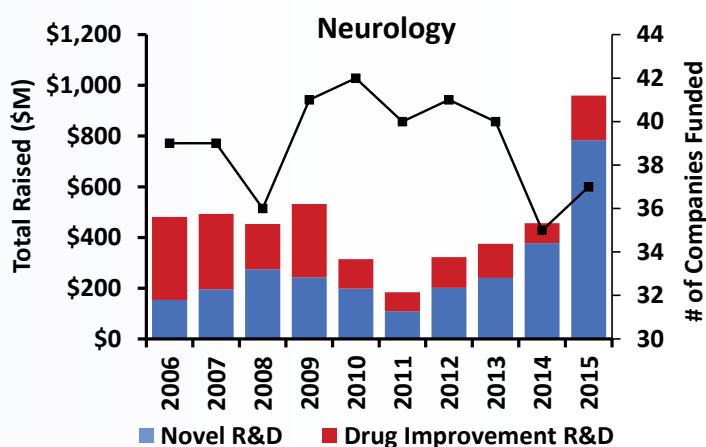
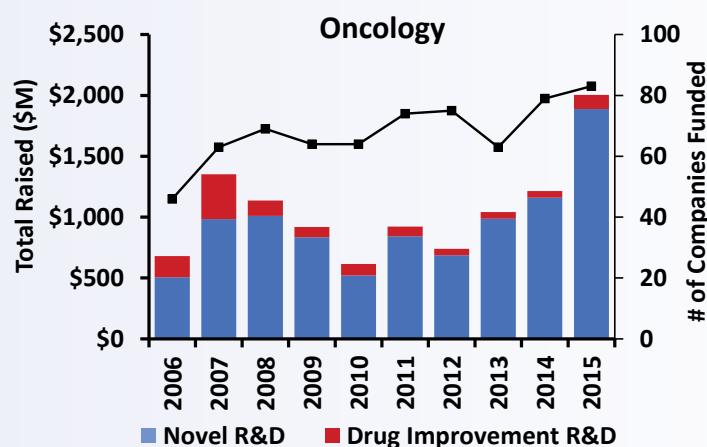
**Chart 5. The percent change in novel venture capital investment by disease between the past two-five year periods (2006-2010 vs. 2011-2015)**

**Table 3** below shows the number of venture financings and the sum total for each year, by disease. In **Chart 6**, these investments are shown broken down by novel R&D vs. improvement R&D investment. Over the last decade, endocrine and neurology have experienced a much higher percentage of improvement R&D investment than most other disease areas. In contrast, oncology and metabolic continue to have mostly novel R&D investment.

Disease Area	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Oncology	46 \$680	63 \$1,353	69 \$1,136	64 \$919	64 \$616	74 \$923	75 \$740	63 \$1,042	79 \$1,215	79 \$2,005
Neurology	39 \$481	39 \$493	36 \$453	41 \$532	42 \$314	40 \$184	41 \$322	40 \$375	35 \$456	37 \$960
Infectious Disease	38 \$522	44 \$596	36 \$435	37 \$452	43 \$323	34 \$383	20 \$167	33 \$350	34 \$535	30 \$574
Other	24 \$283	26 \$370	28 \$266	25 \$225	34 \$320	19 \$206	24 \$367	25 \$282	26 \$332	29 \$420
Platform	23 \$360	25 \$208	35 \$180	24 \$221	32 \$250	23 \$141	27 \$286	29 \$341	36 \$874	22 \$1,019
Endocrine	22 \$430	23 \$398	19 \$209	19 \$176	17 \$77	18 \$279	16 \$284	17 \$157	12 \$305	16 \$372
Metabolic	12 \$288	13 \$239	9 \$93	11 \$162	11 \$176	13 \$241	18 \$371	13 \$265	11 \$161	16 \$442
Respiratory	10 \$157	15 \$237	14 \$169	9 \$106	11 \$154	10 \$106	7 \$65	8 \$60	8 \$59	13 \$210
Cardiovascular	28 \$299	24 \$374	19 \$221	15 \$167	18 \$141	18 \$256	16 \$283	16 \$177	12 \$56	12 \$245
Ophthalmology	13 \$174	16 \$285	11 \$138	18 \$196	15 \$92	15 \$216	13 \$107	21 \$275	15 \$272	12 \$166
Immunology	21 \$265	11 \$77	23 \$310	14 \$157	11 \$152	8 \$57	12 \$148	10 \$171	15 \$262	10 \$258
Hematology	9 \$126	9 \$170	8 \$109	6 \$90	10 \$104	7 \$91	11 \$150	7 \$90	5 \$42	7 \$162
Gastrointestinal	12 \$216	7 \$128	10 \$207	3 \$39	4 \$67	4 \$66	8 \$87	5 \$52	4 \$18	5 \$76
Psychiatry	6 \$129	4 \$56	2 \$36	5 \$50	4 \$39	6 \$58	10 \$111	7 \$44	6 \$154	4 \$39
Total	303 \$4,411	319 \$4,984	319 \$3,959	291 \$3,491	316 \$2,826	289 \$3,207	298 \$3,488	294 \$3,680	298 \$4,742	292 \$6,947

**Table 3. Total number of venture capital deals for each disease group as well as the amount invested by disease from 2006-2015.**

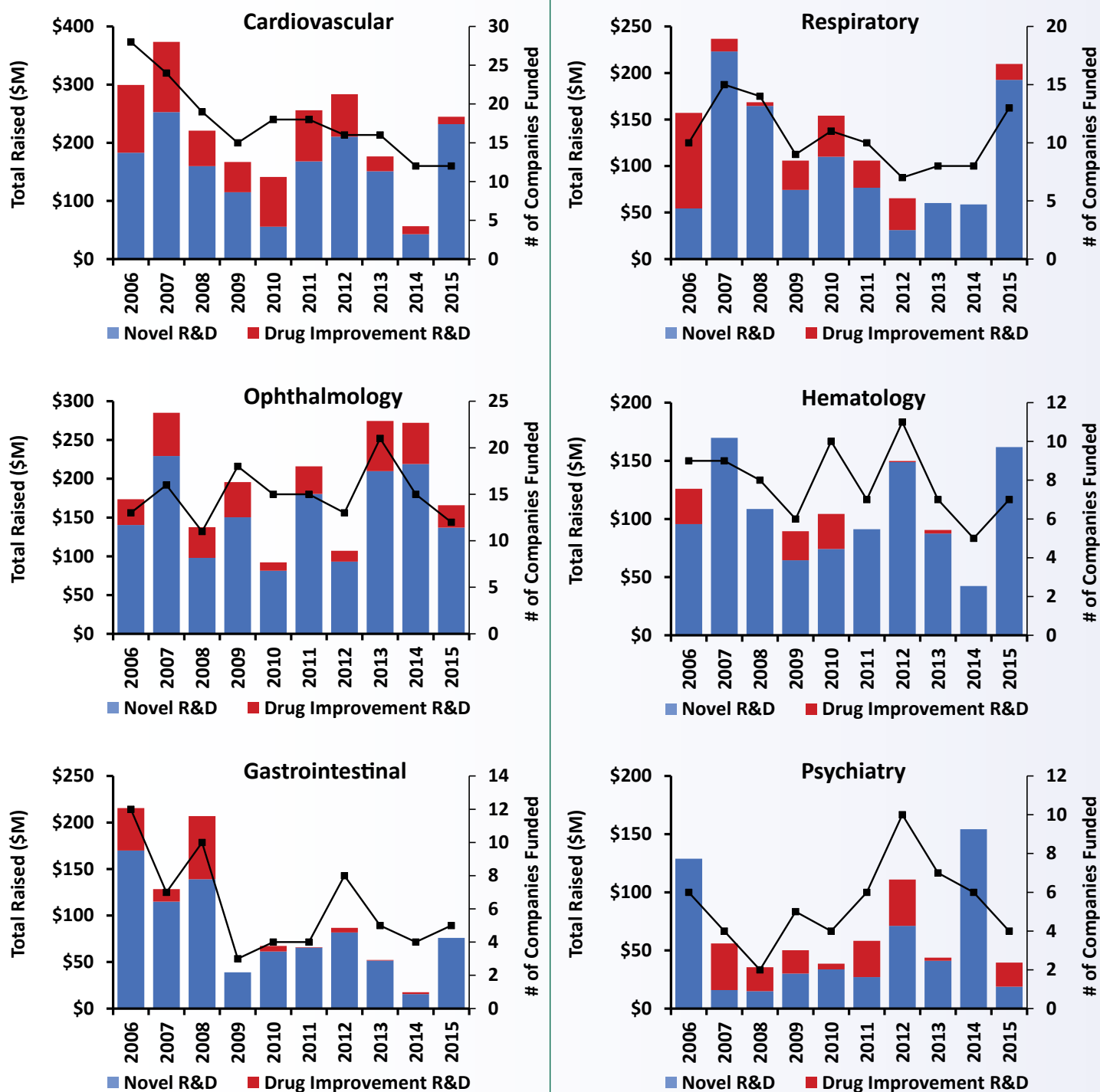
## US Venture Capital by Disease Area



**Chart 6. Total venture funding for each major disease area from 2006-2015. Funding is represented as investment toward R&D of novel molecular entities (blue) vs. improvements of approved drugs (red).**



## US Venture Capital by Disease Area



**Chart 6. Total venture funding for each major disease area from 2006-2015. Funding is represented as investment toward R&D of novel molecular entities (blue) vs. improvements of approved drugs (red).**

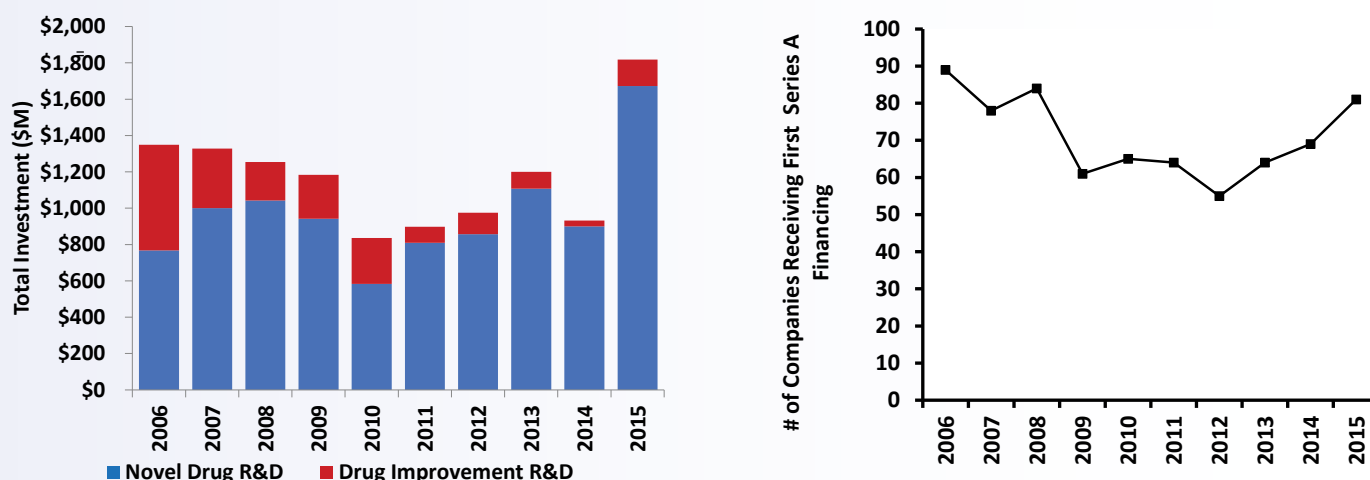
## Series A Venture Funding of US Therapeutic Companies

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. Over the last 10 years, Series A accounted for 23% of the \$52.5 billion invested in all venture rounds. As might be expected, Preclinical companies took in the majority (61%) of Series A venture dollars during this period.

In 2015, we witnessed a resurgence in Series A financing from the drop experienced in 2014. Series A dollars increased from \$932 million in 2014 to \$1.85 billion in 2015, the highest level in biotech history. The level of innovative R&D investment for Series A rounds remained above 90%.

The number of first-time Series A investments also increased substantially, from 69 in 2014 to 81 in 2015. From 2006-2008, prior to the global financial crisis and the resulting exodus of life science investors, the average number of new Series A start-ups per year was 84. After seven long years, the industry is almost back to this level of new company formation.

**SERIES A VENTURE FUNDING OF US THERAPEUTIC COMPANIES, 2006-2015**



**Chart 7. Left: Series A venture funding (\$M) from 2006-2015. Funding is represented as investment toward R&D of novel molecular entities (blue) vs. improvements of approved drugs (red). Right: Number of Companies Receiving First Series A Round, 2006-2015.**

## Series A Venture Funding by Disease

Similar to the totals for all rounds of venture capital by disease group, US oncology took the top spot for both the highest number of Series A deals (42) and total amount invested (\$689 million) in 2015. Both of these numbers are considerably higher than in 2014, with 55% more investment deals and 187% more dollars invested.

When looking at neurology companies, we see that there was only one more Series A transaction in 2015 than in 2014 (14 vs. 13). However, the amount raised in 2015 was more than double the amount raised in 2014 due to a single Preclinical company that received \$217 million to develop large molecule drugs for the treatment of neurodegenerative diseases. As seen in the overall numbers below (**Table 4**), Series A metabolic and rare disease funding were strong in 2015. We did not identify any Series A rounds for companies with lead products in immunology. New start-ups in infectious disease were found to be focused on anti-bacterial and anti-fungal targets more than on anti-viral therapies. New platforms that were funded in 2015 include non-CRISPR gene editing, delivery methods for gene therapy, novel antibody and nucleic acid chemistry platforms.

Disease Area	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Oncology	16 \$120	19 \$238	29 \$290	21 \$324	21 \$135	30 \$250	23 \$99	25 \$372	27 \$240	42 \$689
Neurology	16 \$244	9 \$128	13 \$107	21 \$226	17 \$119	20 \$84	20 \$123	16 \$162	13 \$163	14 \$352
Infectious Disease	15 \$160	23 \$271	18 \$173	12 \$86	17 \$37	9 \$118	9 \$56	10 \$88	10 \$87	14 \$169
Platform	11 \$136	9 \$47	17 \$98	11 \$113	13 \$98	7 \$47	10 \$152	17 \$215	18 \$228	12 \$174
Other	10 \$80	11 \$91	12 \$116	12 \$98	15 \$126	9 \$67	10 \$82	10 \$93	9 \$38	9 \$51
Endocrine	3 \$82	8 \$53	8 \$48	5 \$47	6 \$12	8 \$12	7 \$29	4 \$5	4 \$19	7 \$65
Metabolic	4 \$11	4 \$47	4 \$23	4 \$28	4 \$13	5 \$79	6 \$80	2 \$28	2 \$18	6 \$155
Cardiovascular	16 \$173	9 \$98	7 \$39	6 \$41	8 \$38	8 \$22	7 \$133	6 \$44	5 \$18	5 \$54
Hematology	5 \$73	4 \$36	6 \$40	4 \$26	5 \$45	1 \$2	4 \$54	3 \$35	3 \$37	3 \$21
Psychiatry	2 \$5	2 \$8	0 \$0	1 \$2	2 \$25	3 \$24	4 \$39	4 \$20	1 \$7	3 \$19
Ophthalmology	5 \$85	9 \$156	7 \$71	6 \$49	8 \$45	6 \$92	7 \$59	7 \$113	3 \$26	2 \$8
Respiratory	5 \$96	8 \$90	7 \$52	3 \$22	6 \$62	4 \$50	1 \$3	2 \$0	3 \$8	2 \$34
Gastrointestinal	2 \$5	2 \$9	5 \$48	2 \$9	3 \$64	0 \$0	2 \$16	1 \$15	0 \$0	2 \$27
Immunology	10 \$79	7 \$37	11 \$150	7 \$115	3 \$16	6 \$50	4 \$51	2 \$10	3 \$44	0 \$0
TOTAL	120 \$1,349	124 \$1,308	144 \$1,254	115 \$1,184	128 \$836	116 \$898	114 \$975	109 \$1,201	101 \$932	123 \$1,849

**Table 4. Series A venture funding (\$M) and number of venture transactions by disease area, 2006-2015**

# Initial Public Offerings from US Therapeutic Companies

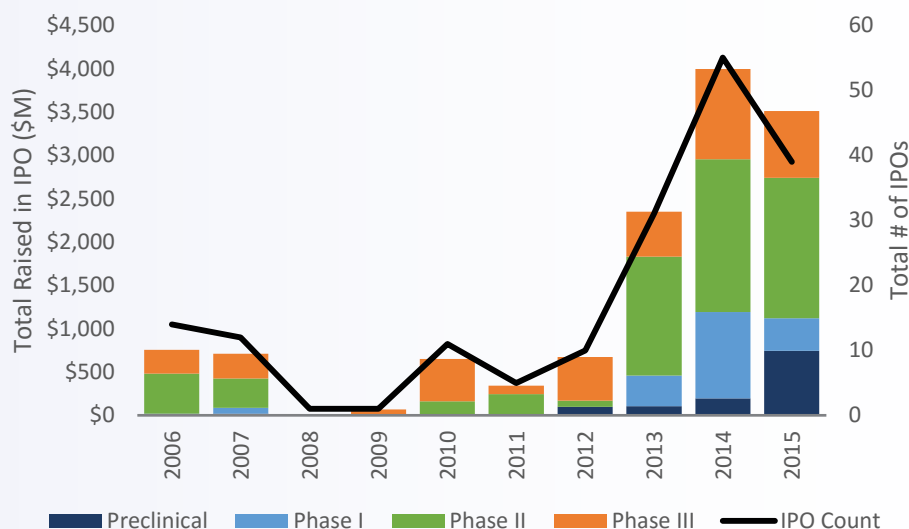
Private emerging companies working on innovative therapeutics are highly dependent on access to capital. For early-stage private companies, the majority of this investment funding comes in the form of venture capital until the eventual listing on a public exchange.

US public financing of emerging therapeutic companies continued to show strength in 2015, with 39 initial public offerings (IPOs). Although a drop from a record 60 in 2014, the healthy showing suggests the strength in IPOs seen since the JOBS Act became law in 2012 continued in 2015. The JOBS Act allowed for enhanced communication between company management and investors prior to filing for a listing on a US exchange and reduced the regulatory cost burden of being a public company.

The average amount raised per offering for R&D-stage companies has gradually increased since the passage of the JOBS Act, from \$66 million in 2012 to \$90 million in 2015. In total, \$10.5 billion was raised by R&D-stage emerging therapeutics companies in the four years between 2012 and 2015, as compared to just \$2.5 billion in the six years between 2006 and 2011.

The clinical development stage emerging companies are in when making the leap onto the public market has changed in recent years. From the start of the financial crisis in 2008 through 2011, there was not a single Preclinical or Phase I IPO in the US, but from 2012 to 2015, 34 made it onto public exchanges. Twelve Preclinical/Phase I therapeutic companies went public in 2015 alone, which represents the largest year for early-stage companies going public in 10 years.

## IPOS FOR US R&D-STAGE THERAPEUTIC COMPANIES, 2006-2015



Stage at time of IPO	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Preclinical - Phase III (#)	14	12	1	1	11	5	10	31	55	39
Marketed (#)	4	3	0	2	1	3	1	1	5	0
Total (#)	18	15	1	3	12	8	11	32	60	39
Preclinical - Phase III (\$M)	\$756	\$711	\$5	\$68	\$650	\$343	\$672	\$2,350	\$3,993	\$3,508
Marketed (\$M)	\$170	\$159	\$0	\$1,035	\$56	\$197	\$55	\$37	\$1,161	\$0
Total (\$M)	\$926	\$870	\$5	\$1,103	\$706	\$541	\$727	\$2,387	\$5,154	\$3,508

**Chart 8. Top: IPOs for US R&D-stage emerging therapeutic companies, by phase, 2006-2015. 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

Similar to venture capital, roughly a quarter of the dollars raised through IPOs went to oncology companies over the past 10 years (\$3.6 billion of the \$15.9 billion raised since 2006). Between 2011 and 2014, oncology companies raised more money through IPOs than any other disease group per year. However, this trend changed in 2015, which saw neurology companies raise \$1.05 billion vs. the \$897 million raised by oncology companies. Neurology companies were largely absent from IPO financing between 2006 and 2013, only raising \$677 million over 8 years. In 2014 and 2015, however, neurology company IPOs raised a total of \$1.5 billion. One notable contribution to the large increase was a single company raising \$315 million to help fund a clinical-stage Alzheimer's program.

Another big change in 2015 was the lack of IPOs from companies in infectious disease and endocrine diseases. Each disease group saw 8 companies go public in 2014 vs. the 2 companies each in 2015. Also, IPOs from companies with lead products in gastrointestinal disease immunology, and platform technologies were completely absent from the 2015 IPO class.

Disease Area	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Neurology	5 \$214	2 \$152	0 \$0	1 \$68	2 \$106	2 \$82	1 \$55	0 \$0	8 \$467	11 \$1,058
Oncology	3 \$104	1 \$50	0 \$0	0 \$0	1 \$81	3 \$248	3 \$236	14 \$958	10 \$1,033	9 \$897
Cardiovascular	0 \$0	0 \$0	1 \$5	0 \$0	2 \$90	0 \$0	0 \$0	2 \$134	3 \$161	3 \$253
Metabolic	0 \$0	2 \$172	0 \$0	0 \$0	0 \$0	0 \$0	1 \$50	3 \$301	2 \$176	3 \$155
Infectious Disease	4 \$202	4 \$172	0 \$0	0 \$0	3 \$123	0 \$0	2 \$140	4 \$315	8 \$420	2 \$211
Endocrine	0 \$0	2 \$155	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	8 \$612	2 \$152
Psychiatry	1 \$60	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	1 \$33	2 \$98
Hematology	1 \$106	1 \$15	0 \$0	1 \$950	0 \$0	0 \$0	0 \$0	3 \$205	3 \$309	2 \$192
Ophthalmology	0 \$0	0 \$0	0 \$0	0 \$0	1 \$72	0 \$0	0 \$0	2 \$234	4 \$267	2 \$201
Other	1 \$37	0 \$0	0 \$0	1 \$85	1 \$30	1 \$106	1 \$81	0 \$0	6 \$1,212	2 \$215
Respiratory	0 \$0	1 \$69	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	1 \$72	0 \$0	1 \$77
Immunology	1 \$60	0 \$0	0 \$0	0 \$0	1 \$17	1 \$50	2 \$120	1 \$73	4 \$302	0 \$0
Gastrointestinal	2 \$144	2 \$86	0 \$0	0 \$0	1 \$188	1 \$55	0 \$0	1 \$25	1 \$60	0 \$0
Platform	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	1 \$45	1 \$70	2 \$102	0 \$0
Total	18 \$926	15 \$870	1 \$5	3 \$1,103	12 \$706	8 \$541	11 \$727	32 \$2,387	60 \$5,154	39 \$3,508

**Table 5. IPOs by US R&D-stage companies, 2006-2015. Amount raised (\$M) and number of deals by disease. Listed by total number of deals in 2015, top to bottom.**

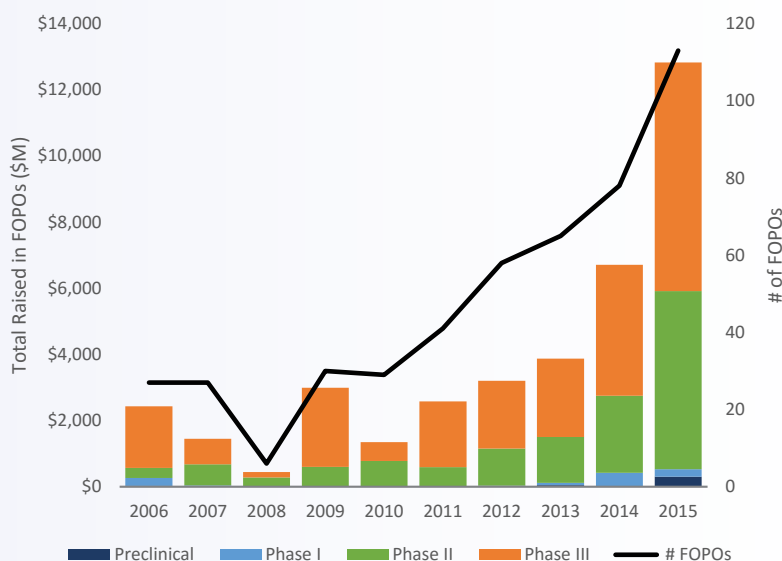
## Follow-On Public Offerings from US Therapeutic Companies

Follow-on public offerings (FOPOs) for US emerging companies grew substantially in 2015, from \$8.9 billion in 2014 to \$16.1 billion in 2015. The majority of this growth can be attributed to pre-market companies raising capital to fund ongoing clinical trials. As shown in **Chart 9**, R&D-stage companies nearly doubled the amount raised in 2015 as compared to 2014 (\$12.8 billion vs. \$6.7 billion).

Another contributing factor is that, out of the 132 FOPO transactions in 2015, 58 raised over \$100 million and 25 raised over \$200 million.

Phase III public R&D-stage therapeutic companies make up more than half of the FOPO dollars raised over the last decade. Some of these companies have been able to raise far more than what they raised in their IPO. Additionally, we can see a steady increase in the number of FOPOs over time.

**FOPOS FOR US THERAPEUTIC COMPANIES, 2006-2015**



Stage at FOPO	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Preclinical - Ph III #, (>\$10M)	27	27	6	30	29	41	58	65	78	113
Marketed #, (>\$10M)	9	7	5	12	16	10	18	24	21	19
Total # (>\$10M)	36	34	11	42	45	51	76	89	99	132
Preclinical - Ph III (\$M)	\$2,431	\$1,453	\$443	\$2,996	\$1,352	\$2,583	\$3,202	\$3,876	\$6,710	\$12,831
Marketed (\$M)	\$1,242	\$608	\$580	\$1,692	\$1,281	\$812	\$1,647	\$2,403	\$2,147	\$3,282
Total (\$M)	\$3,673	\$2,060	\$1,023	\$4,688	\$2,633	\$3,395	\$4,850	\$6,279	\$8,857	\$16,113

**Chart 9. Top: FOPOs for US R&D-stage emerging therapeutic companies, 2006-2015. Bottom: The number of FOPOs (with values above \$10M) and total FOPO dollars raised per year for R&D-stage and market-stage companies, 2006-2015.**



## US Follow-On Public Offerings by Disease

Companies with lead products in metabolic diseases raised the largest share of funding from Follow-On Public Offerings in 2015 (\$3.2 billion). This was a departure from the previous five years, each of which saw oncology companies lead the FOPO pack. Nearly a third of metabolic dollars raised came from only three companies that combined raised nearly \$2 billion. (One market-stage rare disease company raised \$912 million, a rare disease-focused RNAi company raised \$517 million, and a rare disease gene therapy company raised \$500 million.) Of the remaining seven metabolic companies conducting FOPOs in 2015, six raised over \$100 million.

In addition to companies focused on metabolic diseases, there were four additional disease areas that more than doubled the amount raised in 2015 as compared to 2014. These four disease areas were endocrine (\$1.5 billion vs. \$255 million), immunology (\$1.2 billion vs. \$334 million), cardiovascular (\$988 million vs. \$345 million), and psychiatry \$130 million vs. \$11 million). Contributing to this increase in FOPO transaction amounts for these four diseases were 14 deals worth more than \$100 million each.

Disease Area	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Oncology	10 \$474	11 \$791	2 \$174	15 \$1,570	11 \$644	19 \$1,518	28 \$1,782	25 \$2,260	30 \$2,090	38 \$3,246
Infectious Disease	5 \$633	0 \$0	2 \$338	7 \$1,765	11 \$512	9 \$572	9 \$613	16 \$1,049	10 \$1,054	17 \$1,863
Neurology	3 \$157	9 \$625	3 \$242	3 \$115	9 \$463	4 \$238	11 \$531	12 \$423	13 \$1,712	17 \$1,792
Endocrine	4 \$1,018	3 \$92	1 \$51	2 \$181	4 \$140	5 \$249	6 \$657	8 \$538	5 \$255	13 \$1,491
Immunology	2 \$179	2 \$84	2 \$139	4 \$244	2 \$241	1 \$58	1 \$38	3 \$175	3 \$334	10 \$1,215
Metabolic	4 \$664	1 \$109	1 \$81	3 \$173	0 \$0	3 \$170	6 \$662	2 \$254	8 \$949	10 \$3,329
Other	1 \$37	2 \$68	0 \$0	1 \$109	0 \$0	2 \$46	2 \$70	7 \$418	8 \$646	10 \$1,071
Ophthalmology	1 \$52	0 \$0	0 \$0	2 \$155	1 \$62	0 \$0	4 \$146	1 \$11	4 \$284	7 \$442
Cardiovascular	3 \$243	1 \$35	0 \$0	0 \$0	3 \$76	2 \$91	3 \$114	3 \$270	6 \$345	5 \$988
Hematology	2 \$72	1 \$16	0 \$0	1 \$86	2 \$270	2 \$63	1 \$18	4 \$203	5 \$403	4 \$547
Psychiatry	0 \$0	1 \$12	0 \$0	0 \$0	0 \$0	0 \$0	1 \$22	0 \$0	1 \$11	1 \$130
Respiratory	0 \$0	1 \$78	0 \$0	2 \$100	1 \$114	1 \$96	0 \$0	4 \$337	3 \$432	0 \$0
Gastrointestinal	1 \$144	2 \$149	0 \$0	2 \$190	1 \$111	3 \$294	4 \$197	4 \$342	3 \$345	0 \$0
Platform	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0	0 \$0
Total	36 \$3,673	34 \$2,060	11 \$1,023	42 \$4,688	45 \$2,633	51 \$3,395	76 \$4,850	89 \$6,279	99 \$8,857	132 \$16,113

**Table 6. FOPOs, 2006-2015. Amount raised (\$M) and number of deals by disease. Listed by total number of deals in 2015, top to bottom.**

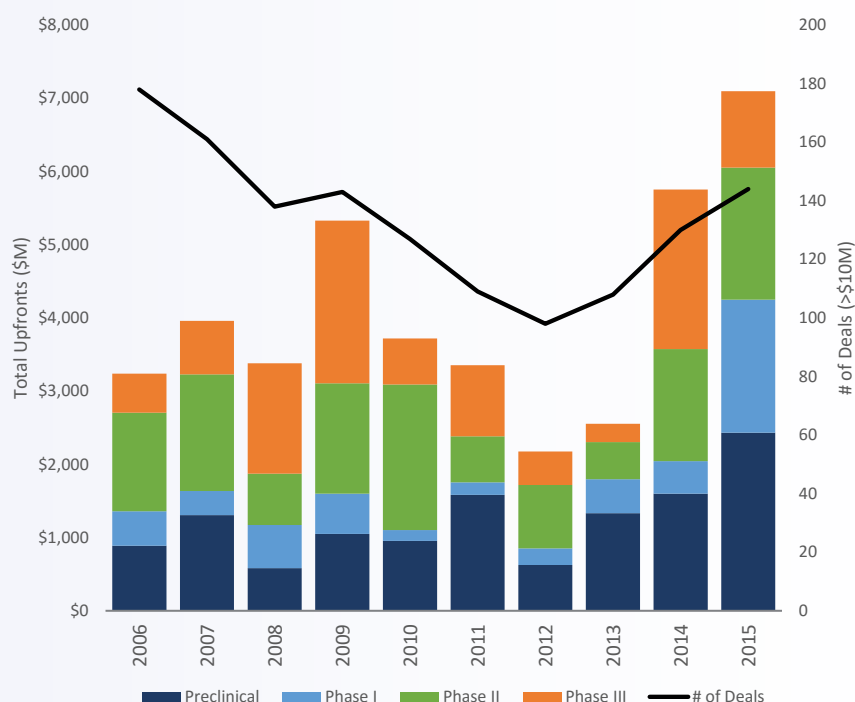
# Global Licensing

For licensing, we focused on R&D-stage assets out-licensed by emerging companies (both US and ex-US) to best represent deal flow and interest from large biopharmaceutical players. In addition to deal count (for deals with more than \$10 million in potential value), we analyzed upfront payments to more accurately reflect actual money flow into small company R&D. Potential payments for regulatory and sales milestones are not included in the numbers below, as many of these payments are not realized due to the challenges faced in drug development. For example, only 16% of drug programs in Phase II will make it to FDA approval (Hay, M., Thomas, D. *Clinical development success rates for investigational drugs*. Nature Biotechnology, January 2014; 32(1):40-51.).

Over the last decade, emerging companies have attracted \$40.5 billion in licensing upfront dollars globally. 2015 had the highest total for upfront dollars in a decade, with \$7.1 billion across 144 deals. Notably, 17 deals had upfront payments over \$100 million; these deals accounted for 70% of the total 2015 upfront payment dollars. The total number of deals in 2015 reached the highest point since 2007, the third consecutive increase since the decade's low point in 2012.

As seen in prior years, Preclinical deals outpaced clinical-stage deals in number, but not in total value of upfront payments. The median preclinical deal upfront in 2015 was \$30 million, as compared to \$50 million for clinical-stage deals.

**GLOBAL LICENSING OF R&D-STAGE THERAPEUTICS, 2006-2015**



Stage at IPO	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Preclinical # of deals >\$10M	90	71	62	60	61	65	50	63	69	78
Clinical # of deals >\$10M	88	90	76	83	66	44	48	45	61	66
Total	178	161	138	143	127	109	98	108	130	144
Preclinical Upfront \$M	\$889	\$1,308	\$582	\$1,052	\$955	\$1,584	\$626	\$1,334	\$1,601	\$2,433
Clinical Upfront \$M	\$2,349	\$2,653	\$2,798	\$4,278	\$2,764	\$1,771	\$1,551	\$1,219	\$4,151	\$4,663
Total	\$3,238	\$3,961	\$3,381	\$5,330	\$3,719	\$3,355	\$2,177	\$2,553	\$5,752	\$7,096

**Chart 10. Top: Global licensing for R&D-stage emerging therapeutics, 2006-2015. Bottom: The number of licensing deals (with values above \$10M) and total upfront dollars per year for R&D-stage companies.**

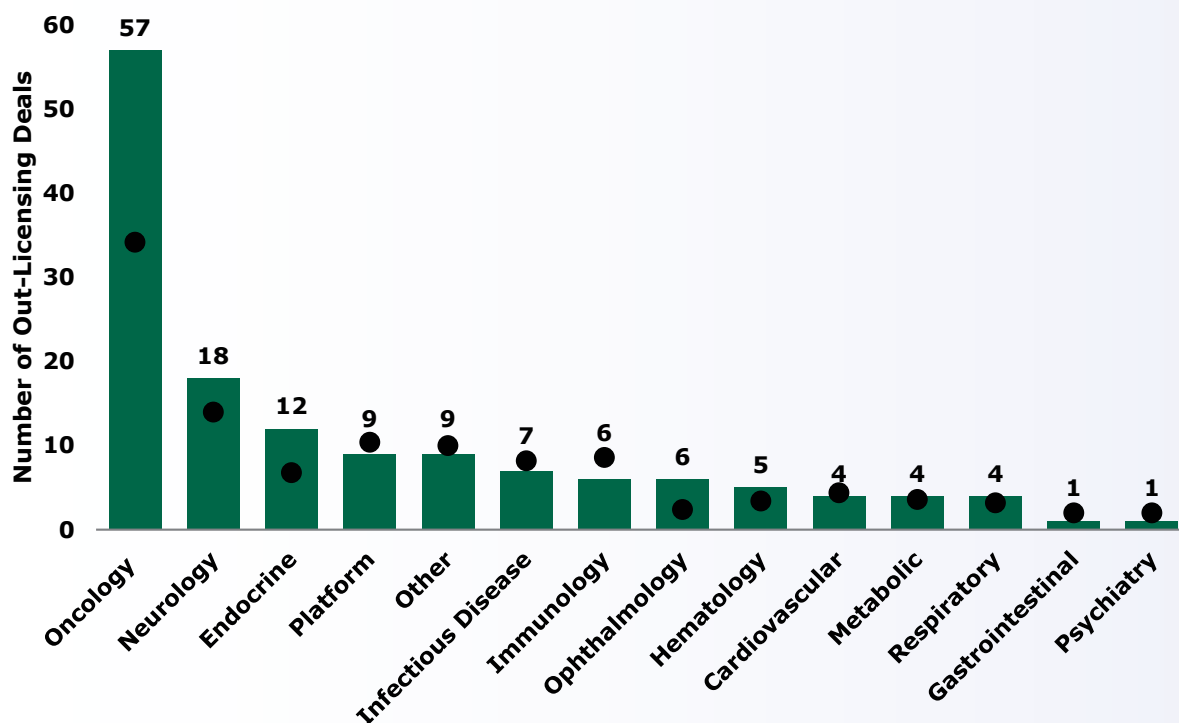
## Global Licensing by Disease

Oncology was not just in the lead for licensing in 2015; it actually jumped to a decade high in both the number of deals and total upfront dollars. To put this in perspective, the \$3.4 billion in upfront payments received for oncology in 2015 was greater than all the upfront payments for all disease areas in 2013 (\$2.5 billion). There were 57 oncology out-licensing deals in 2015 with values above \$10 million. The continued interest in immuno-oncology was a major driver in this increase, and accounted for much of the dollar increase in upfront payments (a jump of 103% over 2014).

Neurology continued to gain interest from large biopharma companies. The 18 out-licensing deals in 2015 were above the annual average of 12 from the preceding five years. Interestingly, the bulk of the \$644 million in 2015 upfront payments came from either Preclinical or very late-stage (Phase III) deals, in Parkinson's disease and treatments for pain.

Endocrine and ophthalmology had double the number of deals compared to their prior five-year annual average. However, both brought in fewer dollars in upfront payments in 2015 vs. 2014. Although there were only four respiratory deals, the upfronts reached a 10 year high at \$380 million.

Fewer immunology and infectious disease deals were signed in 2015 than the average from the previous five years. This slowing in deal flow did not prevent immunology from setting a record level for upfronts (\$898 million) thanks to a single Phase II transaction for rheumatoid arthritis and Crohn's disease.

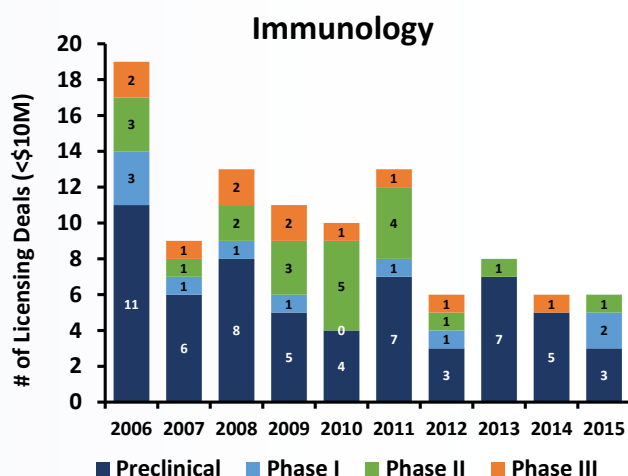
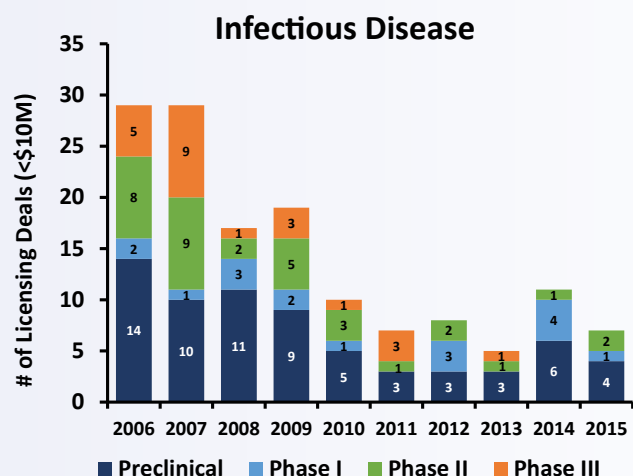
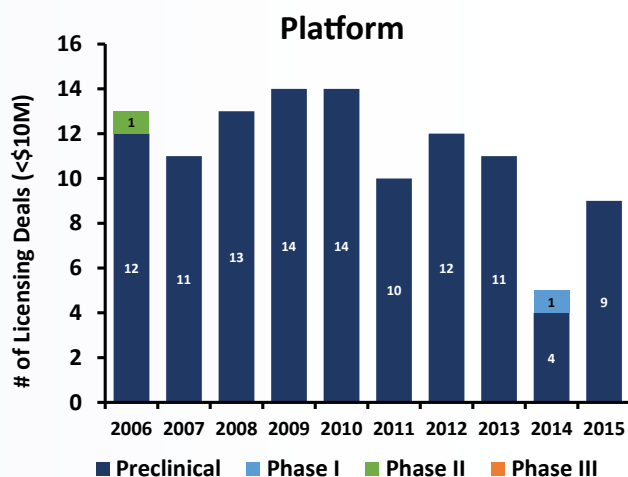
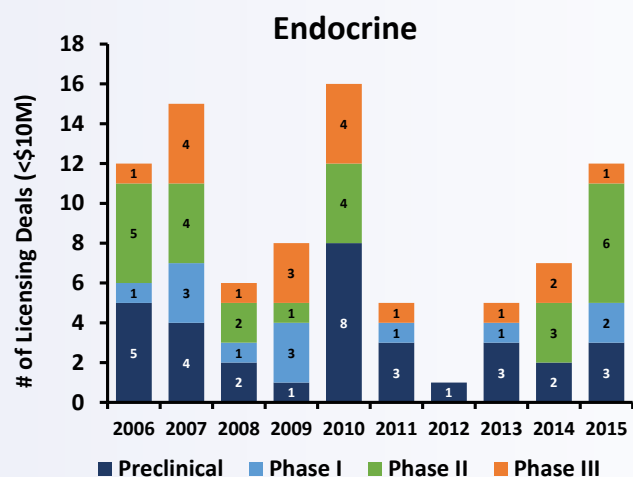
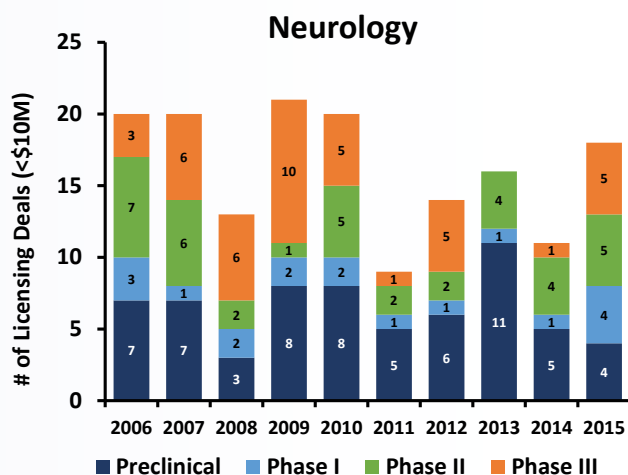
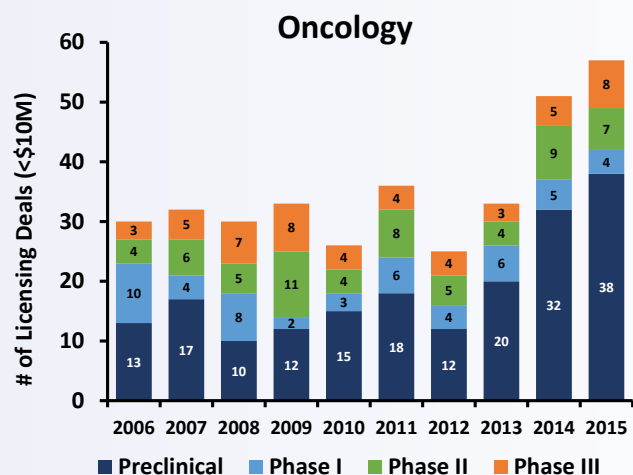


**Chart 11. R&D-Stage Licensing in 2015, by Disease Area, for deals with disclosed value above \$10M. Deals are sorted highest to lowest by number of deals. Black dots represent the previous 5 year average (2010-2014).**

The lowest deal activity for 2015 was in gastrointestinal and psychiatry, which has been the norm over the last five years. With the exception of 2014, when total upfront dollars reached \$798 million (mainly due to one outlier deal with a \$710 million equity upfront), gastrointestinal deal making has slowed heavily since 2009. The same holds true for psychiatric disease deals, where upfronts have remained below \$100 million each year for the last four years.

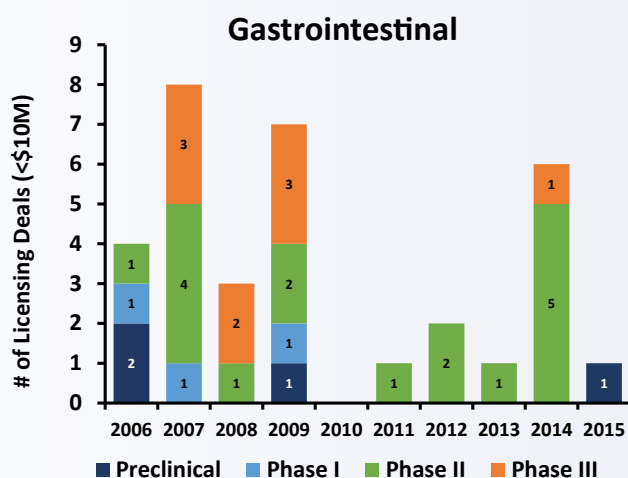
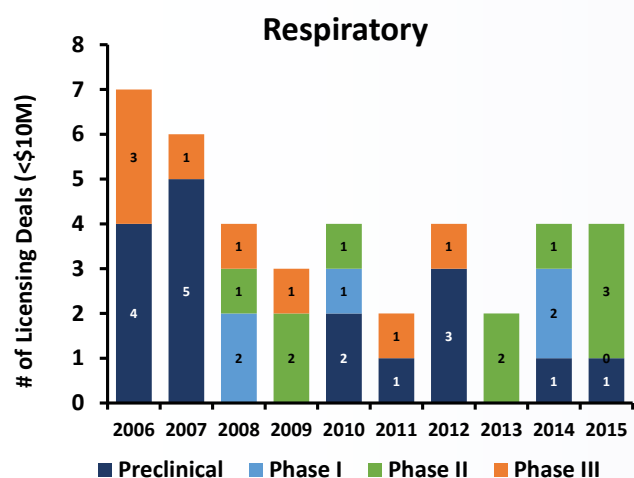
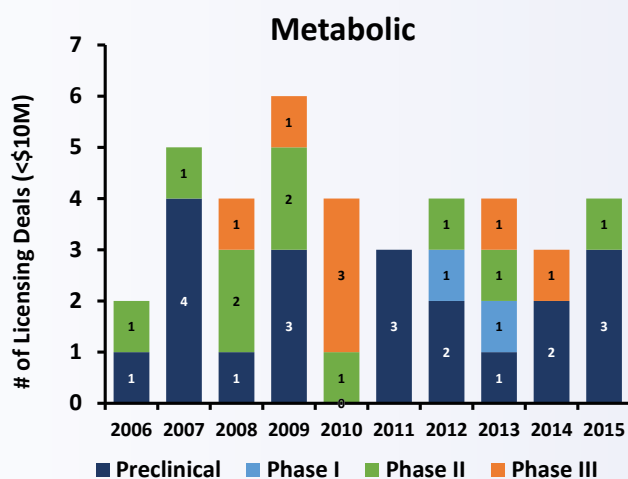
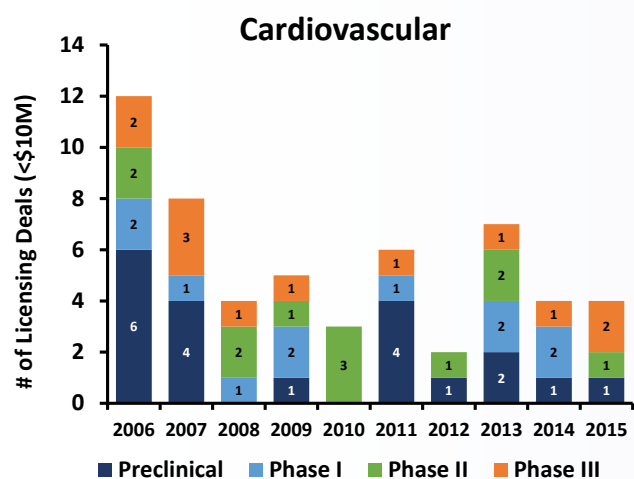
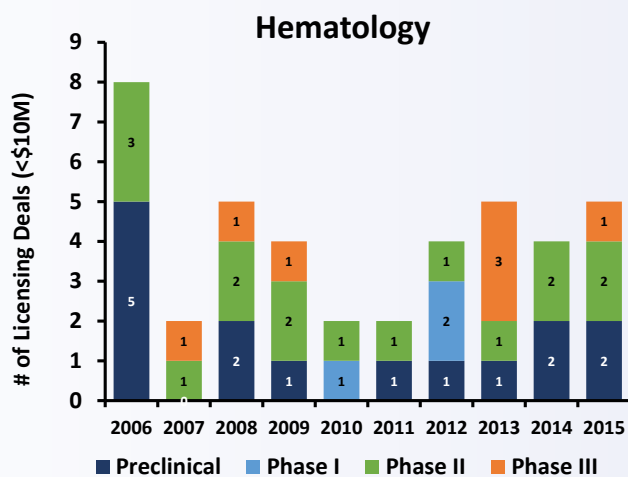
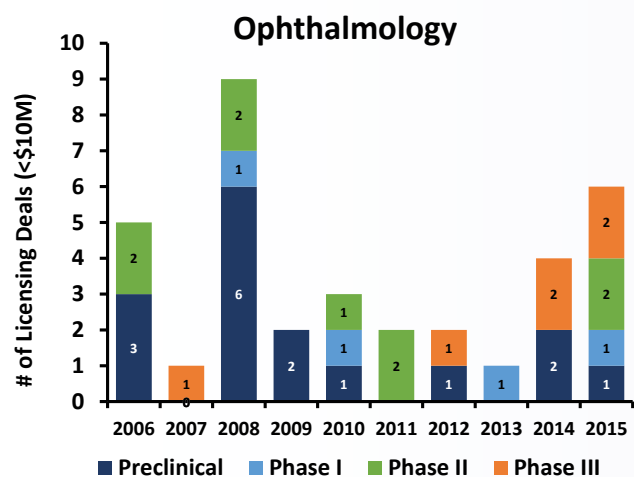
Although reaching its average in deal number in 2015, respiratory reached a decade high in upfront payments with \$380 million. Two deals, both for fibrotic diseases, made up the majority of this cash inflow.

## Global Emerging Company Out-Licensing by Disease, by Phase



**Chart 12. Number of licensing deals with disclosed potential value above \$10M for global emerging therapeutic companies and number of deals by disease, 2006-2015.**

## Global Emerging Company Out-Licensing by Disease, by Phase



**Chart 12. Number of licensing deals with disclosed potential value above \$10M for global emerging therapeutic companies and number of deals by disease, 2006-2015.**

## Global Emerging Company Out-Licensing by Disease

Disease Area	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Oncology	30 \$559	32 \$726	30 \$841	33 \$919	26 \$533	36 \$1,139	25 \$804	33 \$874	51 \$1,677	57 \$3,406
Neurology	20 \$253	20 \$417	13 \$624	21 \$1,559	20 \$251	9 \$128	14 \$231	16 \$276	11 \$586	18 \$327
Endocrine	12 \$125	15 \$354	6 \$138	8 \$113	16 \$476	5 \$588	1 \$8	5 \$96	7 \$530	12 \$377
Platform	13 \$87	11 \$797	13 \$270	14 \$139	14 \$230	10 \$487	12 \$71	11 \$396	5 \$142	9 \$377
Other	15 \$193	11 \$222	14 \$138	5 \$107	10 \$681	9 \$98	12 \$310	7 \$95	12 \$152	9 \$462
Infectious Disease	29 \$570	29 \$717	17 \$218	19 \$797	10 \$304	7 \$197	8 \$257	5 \$58	11 \$196	7 \$56
Immunology	19 \$363	9 \$50	13 \$233	11 \$296	10 \$189	13 \$259	6 \$163	8 \$261	6 \$82	6 \$898
Ophthalmology	5 \$110	1 \$0	9 \$53	2 \$36	3 \$25	2 \$60	2 \$163	1 \$10	4 \$418	6 \$248
Hematology	8 \$511	2 \$75	5 \$19	4 \$102	2 \$30	2 \$25	4 \$38	5 \$66	4 \$260	5 \$230
Cardiovascular	12 \$202	8 \$180	4 \$365	5 \$175	3 \$737	6 \$72	2 \$6	7 \$120	4 \$91	4 \$82
Metabolic	2 \$40	5 \$105	4 \$272	6 \$185	4 \$166	3 \$33	4 \$95	4 \$62	3 \$738	4 \$230
Respiratory	7 \$151	6 \$81	4 \$41	3 \$275	4 \$52	2 \$9	4 \$1	2 \$50	4 \$57	4 \$380
Gastrointestinal	4 \$54	8 \$145	3 \$148	7 \$266	0 \$0	1 \$50	2 \$20	1 \$70	6 \$798	1 \$0
Psychiatry	2 \$20	4 \$93	3 \$22	3 \$231	3 \$32	3 \$202	2 \$11	1 \$98	1 \$25	1 \$10
Total	178 \$3,238	161 \$3,961	138 \$3,381	141 \$5,200	125 \$3,706	108 \$3,347	98 \$2,177	106 \$2,533	129 \$5,752	143 \$7,081

**Table 7. Licensing, amount raised (\$M) for deals with disclosed potential value above \$10M and number of deals by disease, 2006-2015.**



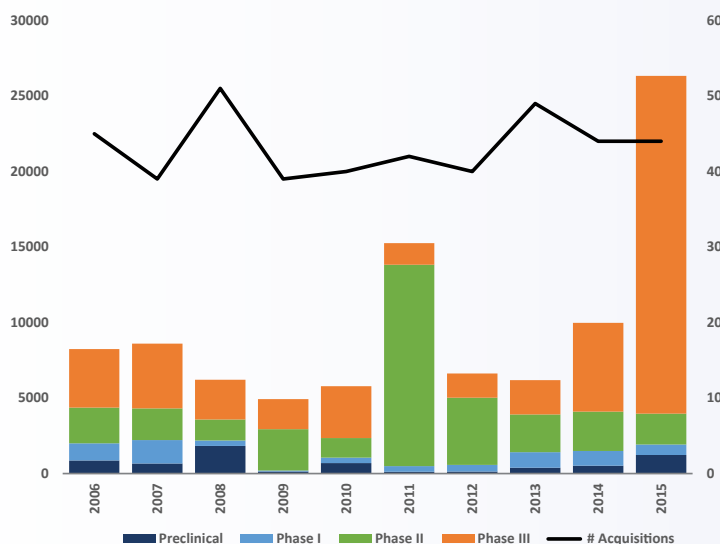
# Global Acquisitions

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.

The number of deals and upfront dollars paid annually for acquiring emerging therapeutic companies worldwide can be seen in **Chart 13**. Global acquisitions of emerging therapeutic companies accounted for \$260 billion in upfront, non-contingent dollars over the last 10 years. Of this total, \$98 billion (38%) was spent on R&D-stage companies. Notably, a large portion of this came in just 2015 alone (\$26.3 billion, breaking the previous high watermark of 2011, which included Gilead's purchase of Phase II Pharmasset for \$11 billion).

Although the total amount paid has been increasing in the last two years, we continue to see the same number of companies acquired each year. In 2015, 44 emerging companies were acquired, on par with the decade average of 43 per year. This pushed the average price paid for an R&D-stage company in 2015 to 2.6 times the average for the last five years (\$823 million vs. \$310 million). The increase in Phase III acquisitions was the notable driver in 2014 and 2015, as a number of multi-billion dollar buyouts occurred after top line Phase III data were made public. The average market-stage acquisition was \$3 billion in 2015.

**GLOBAL ACQUISITIONS OF R&D-STAGE THERAPEUTIC COMPANIES, 2006-2015**



Stage at Acquisition	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
R&D-stage	35	32	36	29	27	27	24	32	33	32
Market-stage	10	7	15	10	13	15	16	17	11	12
Total	45	39	51	39	40	42	40	49	44	44
R&D-stage Upfront (\$M)	\$8,244	\$8,603	\$6,203	\$4,923	\$5,777	\$15,250	\$6,627	\$6,182	\$9,979	\$26,337
Market-stage Upfront (\$M)	\$9,361	\$11,346	\$19,680	\$9,630	\$11,598	\$3,396	\$16,390	\$25,096	\$19,285	\$35,887
Total	\$17,606	\$19,948	\$25,883	\$14,553	\$17,375	\$18,646	\$23,017	\$31,278	\$29,265	\$62,224

**Chart 13. Top: Acquisitions of global emerging therapeutic companies, by phase, 2006-2015. Bottom: The number of acquisitions (with values above \$10M) and total dollars raised per year for R&D-stage and market-stage companies.**

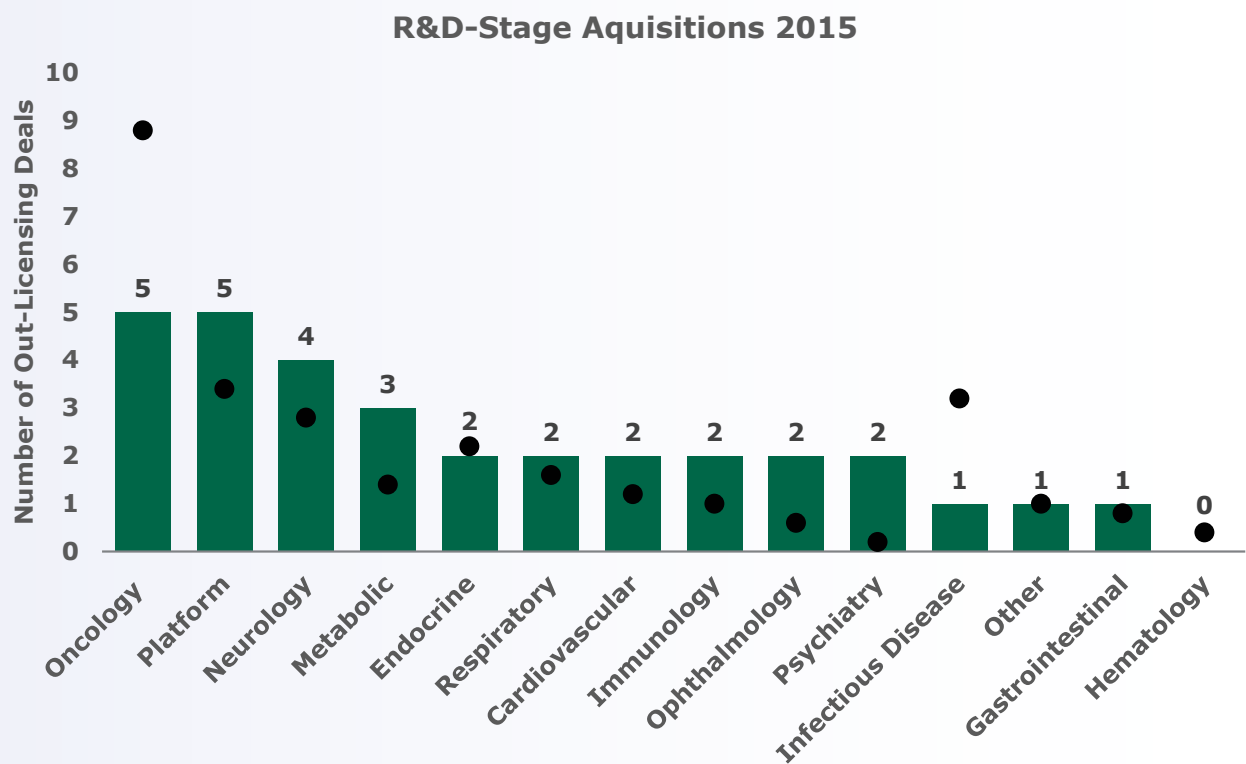
# Global Acquisitions by Disease

Oncology acquisitions were down in 2015 in terms of both dollars and number of transactions. There were five oncology deals in 2015 (below the five-year average of nine) for a total of \$1 billion in upfront payments (below the five-year average of \$1.4 billion). Oncology was the most sought after disease area for licensing, and the acquisition data may be pointing to a strategic move to partner rather than buy entire immuno-oncology pipelines, perhaps due to the sheer breadth of opportunities and possible combo trials, making it easier to diversify interests.

2015 was the biggest year in a decade, in dollar terms, for emerging companies in neurology (\$3.6 billion), endocrine (\$2.7 billion), gastrointestinal (\$7.3 billion), and psychiatry (\$462 million).

Some disease areas have seen just a few transactions per year, but that does not mean that their dollar amounts are insignificant. For example, Synageva, with Phase III data in hand was acquired by Alexion for \$8.5 billion and accounted for 90% of metabolic disease deal upfront payments in 2015. The Celgene acquisition of Receptos last year propelled gastrointestinal deal upfronts to the biggest year in dollar terms.

A sizable drop in activity was seen in infectious disease, with only one acquisition (a bacterial vaccine company). Earlier in the decade, small molecule anti-viral company acquisitions were plentiful, pushing the average number of deals per year above three. However, in recent years, there have been fewer acquisitions of small molecule anti-viral companies.



**Chart 14. R&D-Stage Acquisitions in 2015, by Disease Area, for deals with disclosed value above \$10M. Deals are sorted highest to lowest by number of deals. Black dots represent the previous 5 year average (2010-2014).**

Sixty-six percent of acquisition targets in 2015 were headquartered in the US. Just over 27% were based in Europe (on par with the 10 year average of 26%). Although the global median R&D-stage acquisition upfront payment was \$179 million in 2015, US-based companies saw higher upfronts, with a median of \$229 million. This trend held true for the full potential value of deals – the median potential value for US R&D-stage acquisitions was \$560 million compared to \$429 million for all R&D-stage companies.

Disease Area	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Oncology	9 \$1,098	11 \$5,014	9 \$726	8 \$1,773	4 \$2,833	11 \$2,218	7 \$2,175	10 \$2,616	12 \$1,435	5 \$1,011
Platform	6 \$1,297	5 \$427	7 \$946	1 \$29	8 \$598	1 \$10	3 \$111	2 \$51	3 \$175	5 \$541
Neurology	5 \$581	2 \$327	3 \$81	4 \$703	2 \$695	3 \$210	3 \$46	1 \$37	5 \$952	4 \$3,644
Metabolic	1 \$18	0 \$0	1 \$30	0 \$0	1 \$22	1 \$610	1 \$293	3 \$74	1 \$89	3 \$8,716
Endocrine	2 \$17	3 \$620	0 \$0	0 \$0	3 \$472	1 \$71	1 \$315	3 \$730	3 \$107	2 \$2,722
Respiratory	0 \$0	0 \$0	0 \$0	0 \$0	3 \$204	1 \$328	2 \$178	2 \$600	0 \$0	2 \$260
Cardiovascular	1 \$2,244	1 \$350	2 \$538	2 \$153	1 \$165	1 \$10	1 \$3	2 \$336	1 \$42	2 \$600
Immunology	2 \$68	3 \$933	3 \$1,012	2 \$221	1 \$102	2 \$186	1 \$1,272	0 \$0	1 \$260	2 \$330
Ophthalmology	2 \$1,128	0 \$0	0 \$0	3 \$298	0 \$0	0 \$0	0 \$0	1 \$160	2 \$67	2 \$300
Psychiatry	0 \$0	1 \$29	0 \$0	0 \$0	1 \$226	0 \$0	0 \$0	0 \$0	0 \$0	2 \$462
Infectious Disease	5 \$1,461	4 \$358	5 \$916	6 \$1,187	0 \$0	2 \$11,412	3 \$2,131	7 \$1,339	4 \$5,827	1 \$190
Other	0 \$0	2 \$545	5 \$1,553	2 \$302	1 \$70	3 \$175	1 \$9	0 \$0	0 \$0	1 \$229
Gastrointestinal	2 \$332	0 \$0	0 \$0	0 \$0	2 \$390	1 \$21	0 \$0	0 \$0	1 \$1,027	1 \$7,332
Hematology	0 \$0	0 \$0	1 \$400	1 \$255	0 \$0	0 \$0	1 \$94	1 \$240	0 \$0	0 \$0
Total	35 \$8,244	32 \$8,603	36 \$6,203	29 \$4,923	27 \$5,777	27 \$15,250	24 \$6,627	32 \$6,182	33 \$9,979	32 \$26,337

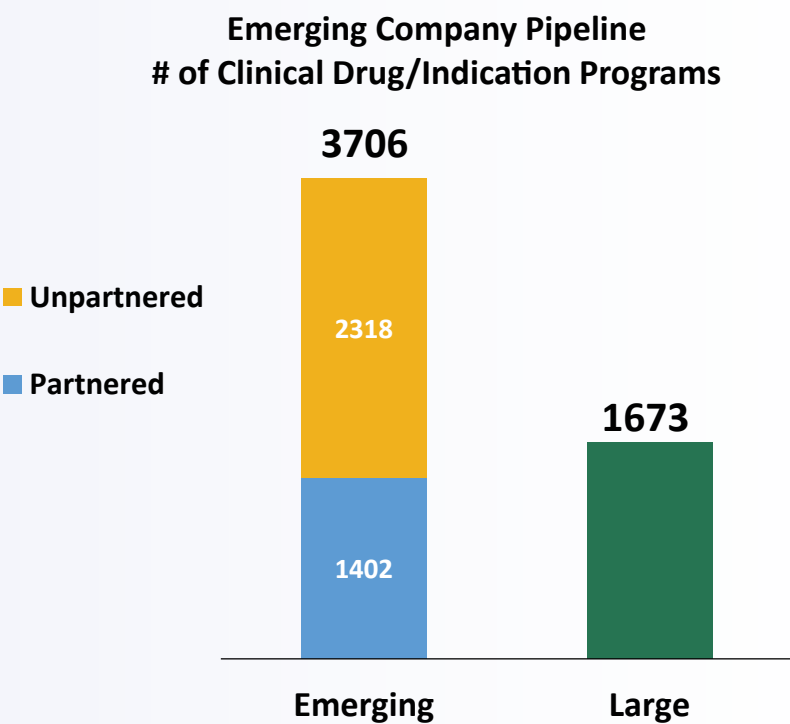
**Table 8. R&D-stage acquisitions, 2006-2015. Both the number of full company acquisitions and the total value of non-conditional acquisition cost is shown in the table, by year, for deals with disclosed potential value above \$10M.**

# Clinical Pipeline

Emerging companies have a robust pipeline, with over 3,700 drug indication programs under development (based on analysis of the BioMedTracker database). This accounts for a full 69% of the entire global industry pipeline, which stands at 5,379 programs. Roughly 43% of emerging company programs are partnered with other companies, demonstrating the importance of licensing and collaborations in the biopharmaceutical industry.

More than half of the emerging company pipeline is in Phase II (55%), and only 16% is in Phase III. However, these late-stage compounds are more likely to be partnered than early-stage assets. For example, only 36% of emerging company programs in Phase I are partnered, whereas 51% in Phase III are partnered.

As it did with investments and licensing over the last decade, oncology made up the largest percentage of the emerging company clinical pipeline (38%), with more than 1,300 drug programs. As shown in **Table 9**, immunology and neurology follow with just over 500 and 400 programs, respectively. Six of the main disease areas (ophthalmology, metabolic, respiratory, psychiatry, hematology, gastrointestinal) had less than 100 clinical programs run by emerging companies, with only a handful in late-stage clinical testing.



**Chart 15.** Number of clinical (Phase I, II, III) Drug/Indication programs in the pipeline at emerging therapeutic companies (blue partnered/ orange unpartnered) and large drug developers (green).

Disease Area	Partnering Status	Phase I	Phase II	Phase III	Total
Oncology	Partnered	177	326	68	571
	Unpartnered	308	386	69	763
Immunology	Partnered	37	119	49	205
	Unpartnered	87	201	56	344
Neurology	Partnered	35	67	30	132
	Unpartnered	103	121	47	271
Other	Partnered	31	53	28	112
	Unpartnered	71	132	49	252
ID	Partnered	20	54	39	113
	Unpartnered	82	86	27	195
Endocrine	Partnered	7	29	10	46
	Unpartnered	41	78	16	135
CV	Partnered	5	31	14	50
	Unpartnered	26	50	10	86
Ophthalmology	Partnered	8	23	6	37
	Unpartnered	10	35	11	56
Metabolic	Partnered	8	16	8	32
	Unpartnered	14	29	11	54
Respiratory	Partnered	7	21	8	36
	Unpartnered	16	21	5	42
Psychiatry	Partnered	10	10	3	23
	Unpartnered	16	26	10	52
Hematology	Partnered	5	12	11	28
	Unpartnered	13	11	7	31
GI	Partnered	0	12	5	17
	Unpartnered	22	13	2	37

Total ETC Partnered	350	773	279	1402
Total ETC Unpartnered	809	1189	320	2318
Total ETC	1159	1962	599	3720
% of ETC partnered	30%	39%	47%	38%
Large Company	571	727	375	1673
Total Pipeline	1730	2689	974	5393
% ETC vs. total pipeline	67%	73%	61%	69%

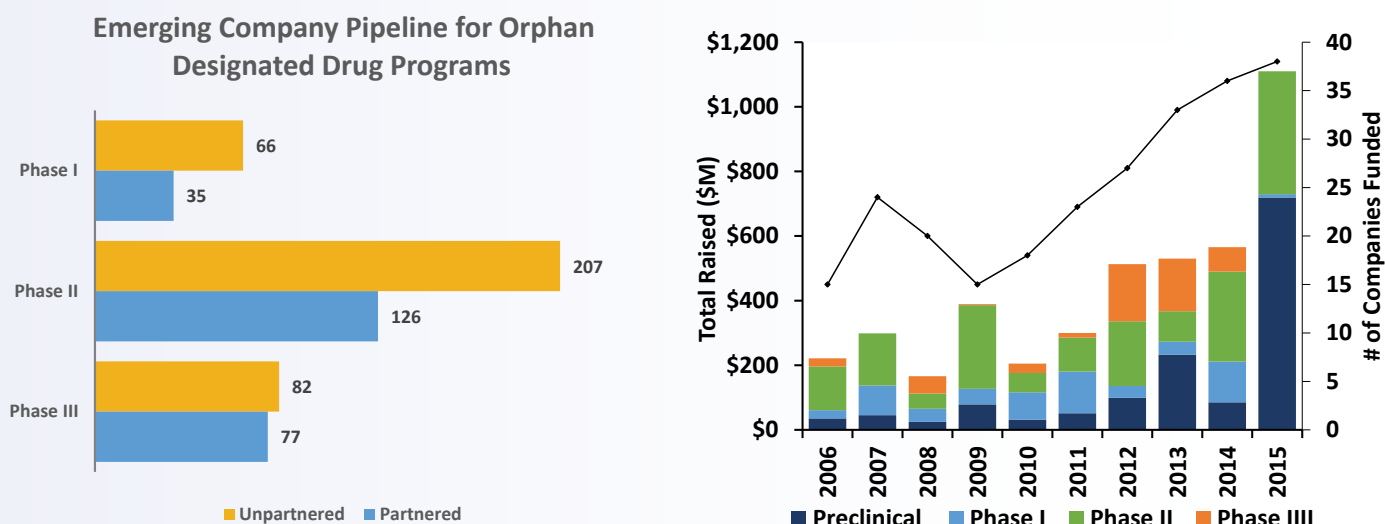
**Table 9. Number of emerging therapeutic company clinical (Phase I, II, III) programs, partnered vs. unpartnered.**  
**Bottom: Percentage of the entire clinical pipeline from small vs. large companies. ETC means Emerging Therapeutic Company.**

# Rare Disease

According to a recent report (<http://globalgenes.org/rare-diseases-facts-statistics>), there are 7,000 rare diseases that cumulatively affect 30 million Americans. Only 350 therapeutics have been 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, with the highest amount seen in 2015 (over \$1 billion). As shown below, most funding was directed to Preclinical companies in 2015, unlike in previous years where there was a mixed allocation across clinical development stages. The number of companies funded has also increased each year since 2010. Just over 10% of Series A financings were for rare disease start-ups.

## US VENTURE FUNDING OF RARE DISEASES, 2006-2015 AND ORPHAN DRUG PIPELINE FOR EMERGING THERAPEUTIC COMPANIES



**Chart 16. Left: Total venture funding (\$M) into companies with a lead drug in a rare disease, 2006-2015. Total Investment by Phase of R&D and Number of companies receiving financing per year for a specific venture round. Right: Clinical pipeline for Orphan Designated products developed by emerging companies (partnered and unpartnered) as of March 2016.**

**IPOs:** Many recent IPOs and FOPOs are from companies pursuing therapies for rare diseases. Eight companies that completed an IPO in 2015 had a lead product for a rare disease. These companies raised \$770 million. This was up from the six rare disease company IPOs that took place in 2014. The largest rare disease company IPO in 2015 was for a gene therapy company working on rare ophthalmology disease, which raised \$161 million.

**Licensing and Acquisitions:** Increases in licensing and acquisitions in the rare disease space have also been seen over the last few years. For example, the total number of rare disease acquisitions from 2011-2015 (33) is up 106% from 2005-2009 (16). Most of these tend to be R&D-stage companies developing products for inherited disorders. There were eight out-licensing transactions (>\$10M potential value) in 2015 vs. 16 in 2014.

**Pipeline:** The pipeline for orphan-designated products developed by emerging companies is shown in **Chart 16**. Of the 593 Orphan programs currently being developed by emerging companies, 47% are in Phase II and 27% are in Phase III. Nearly half of the Phase III programs are partnered.



## Discussion

The aim of this study was to accurately define the levels of investment and deal interest, specifically for emerging therapeutic companies, and to showcase this by both stage of clinical development and disease area. Tracking relative levels of funding by year and across therapeutic areas allows for the identification of strengths and weaknesses across this often fragile ecosystem of drug innovation.

Venture investment into novel drug R&D continues to show diverging interests since the financial crisis of 2008-2009. Most high prevalence disease areas have not seen the strong rebound that other indications, such as oncology and rare disease, have experienced. In fact, respiratory, gastrointestinal, psychiatry, and endocrine have raised less money in the most recent five year period (2011-2015) than the prior five year period (2006-2010). At the extremes, endocrine funding is down by half while metabolic has doubled when comparing the two five-year windows. This suggests there remains a split between haves and have-nots with respect to venture investment in disease areas.

Licensing continues to be an integral part of the emerging biotech story, with 38% of all emerging company clinical programs partnered. When looking just at Phase III programs, where most of the costs are incurred, the percentage partnered is 47%. The degree to which these late-stage programs are partnered was found to vary greatly by disease area, with 71% of gastrointestinal programs partnered, but only 23% of psychiatry programs. In terms of funding, total R&D-stage licensing upfront payments in 2015 (\$7.1 billion) totaled approximately the same as total venture capital raised (\$6.9 billion), further underscoring the role that this non-dilutive funding plays in the biotech sector.

With respect to acquisitions, we continued to see the same number of companies acquired each year, albeit at higher median values in more recent years. In 2015, 44 emerging companies were acquired, on par with the decade average of 43 per year. However, the total paid (ex-Contingent Value Rights) in 2015 for these companies was more than twice the decade average. This is indicative of a competitive environment as large companies continue to diversify their pipelines.

At a higher level, we saw recent acquisition activity targeted towards market-stage and Phase III companies, and licensing more focused more upstream (Phase II and earlier.) With venture capital, the recent surge was in Preclinical, while IPOs were typically targeted towards Phase II and FOPOs were strong with Phase III companies. This is indicative of a balanced flow of financing and deal-making across the varied stages of drug company growth.

Maintaining this 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 are able to 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, 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. 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:** Four databases were combined to create the broadest VC study possible: BioCentury's BCIQ, Informa's Strategic Transactions Database, EvaluatePharma, and Thomson Reuters' ThomsonONE. 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 2006 to 2015 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 tracks IPOs from a variety of news feeds, which includes Biocentury Extra, FierceBiotech, and Renaissance Capital. 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 FOPOs. 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 Recap (Thomson Reuters) 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.

**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	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Oncology - Oncology	\$680	\$1,353	\$1,136	\$919	\$616	\$923	\$740	\$1,042	\$1,215	\$2,005
CV - Hypercholesterolemia	\$6	\$29	\$12	\$2	\$13	\$51	\$16	\$54	\$0	\$118
CV - Hypertension	\$0	\$3	\$10	\$11	\$25	\$3	\$10	\$13	\$1	\$1
CV - Other Indication	\$288	\$332	\$191	\$115	\$93	\$202	\$257	\$109	\$55	\$126
CV - Multiple Indications	\$5	\$10	\$8	\$39	\$10	\$0	\$0	\$0	\$0	\$0
ID - Antimicrobial g+	\$106	\$169	\$31	\$134	\$50	\$74	\$70	\$65	\$101	\$19
ID - Antimicrobial g-	\$13	\$21	\$46	\$2	\$5	\$44	\$9	\$70	\$10	\$41
ID - Antimicrobial broad	\$142	\$87	\$73	\$19	\$114	\$65	\$0	\$28	\$147	\$117
ID - Anti-fungal	\$16	\$6	\$39	\$75	\$6	\$22	\$3	\$41	\$102	\$135
ID - Antiviral - other	\$44	\$97	\$25	\$95	\$20	\$71	\$14	\$55	\$99	\$84
ID - HCV	\$82	\$85	\$89	\$43	\$25	\$12	\$0	\$21	\$13	\$0
ID - HIV	\$56	\$84	\$50	\$16	\$18	\$42	\$15	\$11	\$0	\$15
ID - Vaccine	\$62	\$19	\$82	\$63	\$84	\$53	\$56	\$59	\$36	\$163
ID - Other Indication	\$0	\$29	\$0	\$6	\$1	\$0	\$0	\$0	\$27	\$0
ID - Multiple Indications	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Immunology - Arthritis	\$58	\$56	\$86	\$5	\$29	\$8	\$56	\$0	\$109	\$5
Immunology - Psoriasis	\$0	\$0	\$6	\$2	\$2	\$0	\$11	\$10	\$74	\$18
Immunology - Other Indication	\$115	\$7	\$122	\$106	\$83	\$49	\$70	\$116	\$79	\$187
Immunology - Multiple Indications	\$92	\$15	\$97	\$44	\$38	\$0	\$11	\$45	\$0	\$48
Endocrine - T2D	\$179	\$165	\$138	\$23	\$37	\$180	\$219	\$29	\$229	\$207
Endocrine - T1D	\$51	\$34	\$5	\$16	\$8	\$3	\$0	\$14	\$3	\$33
Endocrine - Other Indication	\$201	\$200	\$66	\$138	\$32	\$96	\$65	\$114	\$74	\$132
Endocrine - Multiple Indications	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Metabolic - Obesity	\$55	\$7	\$37	\$11	\$32	\$73	\$21	\$35	\$12	\$43
Metabolic - Genetic Disorder	\$63	\$92	\$29	\$100	\$31	\$133	\$235	\$97	\$135	\$339
Metabolic - Other Indication	\$47	\$96	\$19	\$51	\$113	\$35	\$115	\$133	\$14	\$12
Metabolic - Multiple Indications	\$122	\$44	\$8	\$0	\$0	\$0	\$0	\$0	\$0	\$48
Psychiatry - Schizophrenia	\$56	\$14	\$0	\$2	\$0	\$0	\$19	\$18	\$17	\$0
Psychiatry - Depression	\$23	\$2	\$36	\$4	\$38	\$27	\$75	\$7	\$121	\$4
Psychiatry - Other Indication	\$50	\$40	\$0	\$44	\$0	\$31	\$17	\$19	\$16	\$36
Psychiatry - Multiple Indications	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Neurology - Pain	\$283	\$266	\$158	\$245	\$124	\$106	\$161	\$97	\$137	\$159
Neurology - Parkinson's	\$8	\$28	\$0	\$0	\$26	\$10	\$15	\$39	\$117	\$196
Neurology - Alzheimer's	\$17	\$15	\$44	\$47	\$48	\$31	\$34	\$54	\$28	\$105
Neurology - MS	\$20	\$48	\$129	\$40	\$2	\$9	\$17	\$21	\$5	\$0
Neurology - Other Indication	\$102	\$134	\$31	\$181	\$66	\$21	\$78	\$134	\$169	\$282
Neurology - Multiple Indications	\$51	\$2	\$91	\$19	\$50	\$8	\$18	\$30	\$0	\$217

**A1. Venture capital, by sub-indication (\$M invested per year), 2006-2015.**

# Appendix

Disease - Subindication	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Respiratory - Asthma	\$56	\$137	\$39	\$52	\$31	\$9	\$3	\$6	\$38	\$4
Respiratory - COPD	\$6	\$37	\$20	\$0	\$59	\$49	\$53	\$42	\$0	\$0
Respiratory - Other Indication	\$95	\$56	\$106	\$22	\$65	\$34	\$6	\$13	\$21	\$206
Respiratory - Multiple Indications	\$0	\$8	\$4	\$32	\$0	\$14	\$3	\$0	\$0	\$0
Hematology - Blood Stimulator	\$26	\$129	\$3	\$3	\$22	\$52	\$63	\$3	\$0	\$0
Hematology - Coagulation	\$69	\$0	\$40	\$25	\$22	\$0	\$7	\$11	\$32	\$93
Hematology - Other Indication	\$29	\$34	\$65	\$56	\$60	\$39	\$80	\$77	\$10	\$69
Hematology - Multiple Indications	\$2	\$6	\$0	\$6	\$0	\$0	\$0	\$0	\$0	\$0
GI - IBS	\$84	\$97	\$85	\$39	\$18	\$30	\$30	\$26	\$11	\$18
GI - GERD	\$30	\$0	\$5	\$0	\$0	\$0	\$0	\$0	\$0	\$0
GI - Crohn's	\$66	\$3	\$105	\$0	\$0	\$0	\$16	\$0	\$0	\$38
GI - Ulcerative Colitis	\$6	\$2	\$6	\$0	\$0	\$0	\$19	\$1	\$2	\$0
GI - Other Indication	\$30	\$26	\$6	\$0	\$49	\$35	\$22	\$26	\$5	\$0
GI - Multiple Indications	\$0	\$0	\$0	\$0	\$0	\$1	\$0	\$0	\$0	\$20
Ophthalmology	\$174	\$285	\$138	\$196	\$92	\$216	\$107	\$275	\$272	\$166
PLATFORM	\$360	\$208	\$180	\$221	\$250	\$141	\$286	\$341	\$874	\$1,019
Other - Allergy	\$6	\$0	\$0	\$0	\$0	\$0	\$0	\$29	\$41	\$93
Other - Dermatology	\$90	\$60	\$49	\$62	\$81	\$80	\$72	\$110	\$120	\$146
Other - Renal	\$98	\$68	\$67	\$53	\$71	\$27	\$103	\$45	\$70	\$81
Other - Chemo/Rad side effects	\$0	\$33	\$0	\$10	\$20	\$44	\$58	\$0	\$0	\$0
Other - Other Indication	\$53	\$109	\$52	\$47	\$84	\$35	\$134	\$51	\$100	\$84
Other - Multiple Indications	\$36	\$100	\$97	\$53	\$64	\$19	\$0	\$46	\$0	\$16
Total	\$3,731	\$3,631	\$2,823	\$2,572	\$2,210	\$2,284	\$2,748	\$2,638	\$3,527	\$4,942

**A1. Venture capital, by sub-indication (\$M invested per year), 2006-2015.**



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