

US Venture Capital and Public Offerings, 2005-2014 Global Licensing and Acquisitions, 2005-2014 Current Pipeline for Emerging Companies

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



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

June 1, 2015

For small therapeutic-focused biotechnology companies, the ability to access capital and form strategic alliances is vital to maintaining an innovative pipeline. As the world's largest biotech trade association, representing biotechnology companies across the United States and in more than 30 other nations, it is important for BIO to better understand 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.

In this report, we set out to highlight five investment and deal-making activities made exclusively by emerging therapeutic companies: venture capital, IPOs, follow-on public offerings, licensing, and acquisitions. Also, we analyze the degree of collaboration across the industry's clinical pipeline. Part I of the report covers these five categories for emerging therapeutic companies over the last decade, with data broken down by phase of development. Some of the key findings from Part I of this report are:

- Venture Capital: A decade high in 2014 for US venture capital in Novel R&D lead programs. However, Series
  A investments went to fewer companies and with fewer dollars vs 2013. Additionally, some disease areas
  affecting large populations continue to see declines.
- IPOs: A decade high in 2014 for US emerging company IPOs.
- Follow-On Offerings: A decade high in 2014 for US emerging company follow-on offerings.
- Licensing: A decade high in 2014 for upfront payments in R&D-stage licensing deals.
- Acquisitions: R&D-stage acquisition volume is returning to levels not seen since 2008.
- Pipeline: Nearly 70% of the industry clinical pipeline is attributed to small emerging companies. A significant portion of the emerging company pipeline (43%) is partnered.

In Part II of the report, we provide a more in-depth look at the major disease categories for drug R&D. This section allows us to gauge interest levels across the five investment and deal-making activities with respect to each therapeutic area.

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,

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# **Table of Contents**

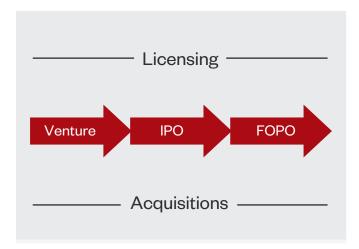
| Part I – Frends by Phase of Development |    |
|---|----|
| Introduction                            | 2  |
| Venture Capital                         |    |
| IPOs                                    | 6  |
| Follow-on Offerings                     |    |
| Licensing                               | 3  |
| Acquisitions                            |    |
| Pipeline                                | 10 |
| Part II - Trends by Disease Areas       |    |
| Overview - US Investment                | 12 |
| Overview - Global Deals                 | 13 |
| Oncology                                | 12 |
| Infectious Disease                      | 16 |
| Neurology                               | 18 |
| Psychiatry                              | 20 |
| Endocrine                               | 22 |
| Metabolic                               | 24 |
| Cardiovascular                          | 26 |
| lmmunology                              | 28 |
| Gastrointestinal                        | 30 |
| Respiratory                             | 32 |
| Hematology                              | 34 |
| Ophthalmology                           | 36 |
| Other                                   | 38 |
| Platform                                | 4C |
| Rare Disease                            | 4  |
| Discussion                              | 42 |
| Mathadalagy                             | 1/ |

#### PART I:

# Emerging Therapeutic Company Investment and Deal Trends by Phase of Development 2005-2014

#### 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 offerings (FOPOs), licensing, and acquisitions. Part I of the report covers each of these five categories broken down by phase of development, year by year over the last decade (2005-2014). In addition, clinical pipeline snapshots are provided to give context on the degree of industry partnering and contribution of emerging companies. Part II provides a more in-depth look at these investment and deal-making areas by segmenting the data into major disease categories. This broadbased 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 development and lead therapeutic category for US companies.

The inclusion of licensing and acquisitions aims to shed light on where the disease focus has been for global drug developers seeking innovation from emerging companies. For licensing, we focus on R&D-stage assets outlicensed by emerging companies to best represent deal flow and interest from large biopharmaceutical players, and to assess how much financial impact this has in a particular space. This means regional marketing deals for approved products are not presented, as their inclusion would blur the allocation to early-stage assets in a given therapeutic area. In addition to the licensing deal numbers, we provide a snapshot of the emerging company partnered and unpartnered pipeline for each disease area.

For licensing and acquisition data, we only report upfront payments to more accurately reflect the actual money flow into small company R&D (licensing) or to investors (acquisition). Typical licensing structures tend to have most of their value "back loaded" based on possible future events (such as regulatory and sales milestones), many of which are never realized due to the challenges faced in drug development. Similar structures are now being used extensively in emerging company acquisitions (66% in our dataset). It has been estimated that the actual payout for these contingent value rights (CVRs) is less than 40%.1 In contrast, the upfront dollars are an immediate, guaranteed commitment from the partner or acquirer.

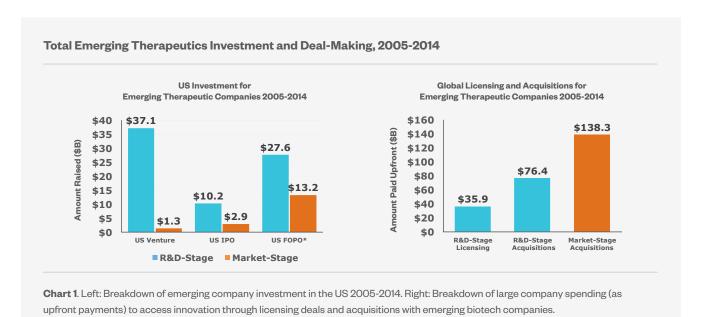
The data presented for acquisitions includes both "R&D-stage" emerging companies (with a lead product in preclinical, Phase I, II, or Phase III), and "market-stage" emerging companies (with an approved product but with under \$1 billion in product sales). By focusing only on small companies, this data may differ from other currently available reports that often include large company acquisitions.

We analyzed data from 2005 through 2014 from five databases to create the broadest, most comprehensive study possible. Each transaction was categorized by each company's lead research focus at the time of investment or deal announcement by phase of development and disease.

## 10 years of emerging company investment and deal making

Over the last decade, a total of \$92.3 billion in investment dollars went into US emerging therapeutic companies through venture capital (42%), follow-on public offerings (44%), and initial public offerings (14%). As will be shown in the following pages, this has been anything but consistent between years. However, the totals here demonstrate the importance of venture for early-stage companies prior to reaching proof of concept, and the need for efficient public markets when proof of concept has been achieved and new capital is needed to run a registration clinical trial or prepare for commercialization.

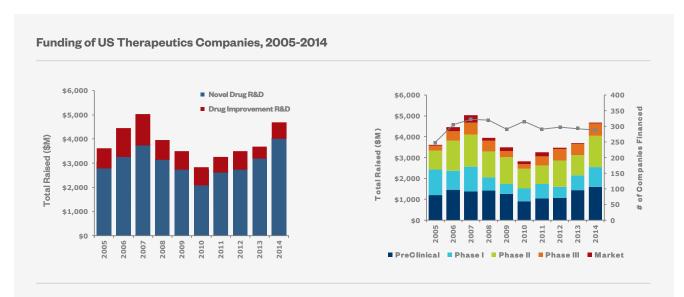
Global R&D-stage emerging companies have attracted \$35.9 billion in licensing upfront dollars over the last 10 years, approaching levels seen with US venture capital. Acquisition upfronts for R&D-stage emerging companies totaled \$76.4 billion. Although this is twice as much as licensing, it is close to half of what is seen for market-stage company acquisitions which totaled \$138.3 billion.



# Venture Capital Funding of US Therapeutic Companies

Venture capital investments in this report are categorized in three ways. First, we differentiate investments 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. Second, we break down investment dollars into the five phases of drug development: Preclinical; Clinical Phases I, II, and III; and marketed product. Third, we break down investment dollars by disease area, which is outlined in Part II of this report.

As shown in Chart 2, venture equity funding of private drug development companies peaked in 2007 with \$4.98 billion in total funding. Although 2014 was a big year, and the fourth consecutive year of increase, the overall total (\$4.68 billion) did not quite reach the 2007 peak. When comparing the relative amount of financing for novel drug R&D vs. drug improvement R&D, we found that 2014 actually did reach a decade high for novel investment (\$4.0 billion).



**Chart 2.** Total venture funding 2005-2014. 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 Drug Development.

Novel Drug R&D = R&D pursuing new chemical entities to treat disease, with no prior regulatory approval.

**Drug Improvement R&D** = R&D that improves upon existing therapeutics, such as new delivery methods, new formulations, or using approved drugs for new indications. Examples: Drug delivery patch, topical cream, implanted delivery device, needle-less injection, extended release, prolonged half-life chemical modifications (conjugations, including pegylated variants), and reformulations of approved drugs.

# 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. In total, \$10.9 billion went into Series A over the last 10 years, which is 28% of the \$38.5 billion invested in all rounds.

As might be expected, Preclinical-stage companies took in the majority (56%) of Series A venture dollars between 2005 and 2014, and "early-stage" R&D, as defined as Preclinical to Phase I, made up 74% of Series A venture investment.

Despite the strong year for later-round deals, 2014 saw a drop in Series A funding. Series A round investment dropped from \$1.2 billion in 2013 to \$0.9 billion in 2014. The number of first-time Series A investments also dropped, from 63 in 2013 to 62 in 2014, which is near the average level since 2009. From 2005-2008, the average number of new companies launched at the Series A stage was 80. Some of this decline may be attributable to the fact that the industry saw an exodus of biotech venture investors during the financial crisis, many of whom have not returned to investing in the industry.

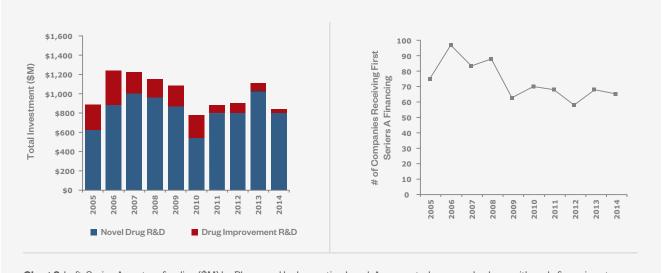


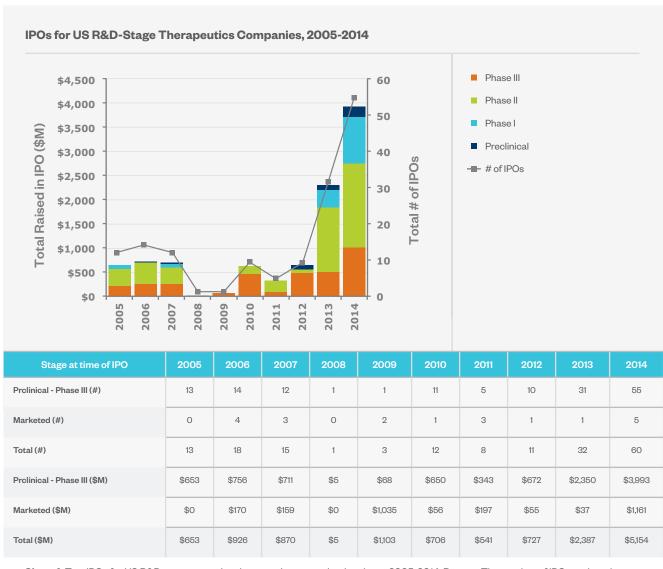
Chart 3. Left: Series A venture funding (\$M) by Phase and by Innovation Level. As expected more early phase with early financing stage. Right: Number of Companies Receiving First Series A Round, 2005-2014.

# **US Initial Public Offerings (IPOs)**

Public company financing of emerging therapeutic companies has been rebounding from a multi-year deep freeze. For initial public offerings (IPOs), this means venture capitalists now have another exit option and companies can access public capital more efficiently. The surge began in early 2013 following enactment of the JOBS Act in 2012, which allowed for enhanced communication between company management and investors prior to filing for a listing on a US exchange. Portfolio managers also gained more confidence in the sector in the years following the financial crisis, as biotech pipelines gave rise to new, transformative products.

The development stage of emerging companies making the leap onto the public stage has changed in recent years. Between 2008 and 2011, there was not a single Preclinical/Phase I IPO in the US, but in the following three years 22 made it onto public exchanges. The average amount raised for a R&D-stage company since the start of 2012 is \$72 million, significantly higher than the \$50 million average in the earlier three year window of 2005 to 2007.

In total, \$7.0 billion was raised by R&D-stage emerging therapeutics companies between 2012 and 2014, vs just \$2.1 billion between 2005 and 2007. The percent change in dollars over these periods is far greater for IPOs than that seen with venture capital.



**Chart 4**. Top: IPOs for US R&D-stage emerging therapeutic companies, by phase, 2005-2014. Bottom: The number of IPOs and total dollars raised per year for R&D-stage and market-stage companies.

# US Follow-On Public Offerings (FOPOs)

The fact that companies can now raise additional capital through an IPO has been positive for backlogged private company investors that were without an exit option and had limited new sources of private capital. Also beneficial to the industry's innovative companies and their investors are the benefits available after reaching the public market. Once public, companies typically observe immediate re-valuation upon the release of new clinical data. When this data is positive, and markets are operating efficiently, companies can file for a follow-on public offering (FOPO) to raise funds for the next stage of develoment.<sup>3</sup>

As can be seen in Chart 5 below for public R&D-stage therapeutic companies, Phase III filers for FOPOs make up more than half of the dollars raised in a given year. Some of these companies have been able to raise far more than what they raised in their IPO. What is also apparent is the steady increase in the number of FOPOs of more than \$10 million. The table below shows that market-stage emerging therapeutics companies (those with under \$1 billion in sales) represent a significant percentage of the total dollars raised via FOPOs. They account for a third of dollars raised and a fourth of the number of offerings of over \$10 million in size.



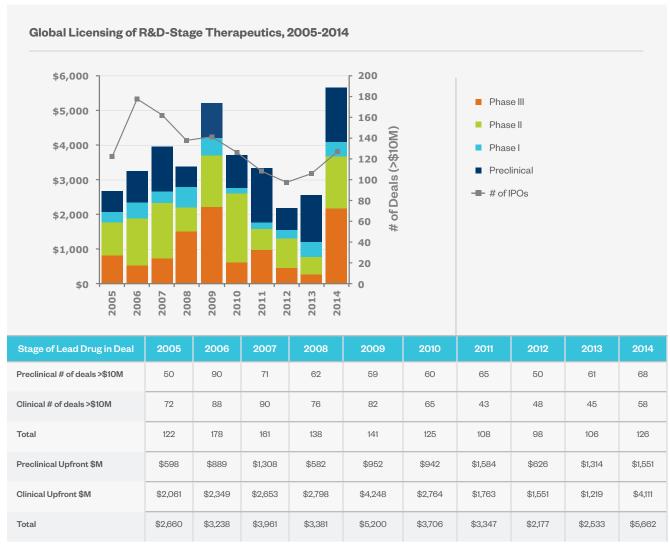
**Chart 5**. Top: US FOPOs for R&D-stage emerging therapeutic companies, by phase, 2005-2014. Bottom: The number of FOPOs (with values above \$10M) and total dollars raised per year for R&D-stage and market-stage companies.

# Licensing of R&D-Stage Therapeutics

Over the last decade, global emerging companies have attracted \$35.9 billion in licensing upfront dollars. These upfront payments typically represent a small portion of an overall licensing agreement (10-20% on average), but are the only guaranteed portion. Typically, development and regulatory objectives are set as milestones for future payment, along with sales targets and royalties. However, the probabilities in the industry are such that many of these milestones are never realized. Thus, measuring deal flow using upfront payments, although imperfect, provides a perspective on large company interests and emerging company funding across disease areas.

After many years of lower aggregate upfront flow, 2014 broke that trend with \$5.6 billion in upfront licensing payments. To put that in perspective, 2014 saw more than a 100% increase from 2013 and the highest total in a decade. Deals with very large upfront payments (over \$100 million) accounted for 64% of the total 2014 upfronts.

The number of out-licensing deals (with potential value above \$10 million) has also rebounded in recent years after declining for most of the decade. However, the 126 deals in 2014 remains well below the peak of 178 deals in 2006, which coincided with a surge in large company interest in pipeline externalization ahead of major patent expirations.



**Chart 6.** Top: Global licensing for R&D-stage emerging therapeutic companies, by phase, 2005-2014. Bottom: The number of licensing deals (with values above \$10M) and total dollars raised per year for R&D-stage and market-stage companies.

## **Acquisitions**

Global acquisitions of emerging therapeutics companies accounted for \$208 billion in upfront, non-contingent dollars, over the last 10 years. Of this, \$131 billion (63%) was spent on emerging companies with marketed products, and \$76 billion (37%) on R&D-stage companies. Acquisition dollars presented in this report are based on upfront payments, as there has been an increased trend toward deal-like structures with acquisitions of small biotech companies. 1

The number of deals and upfront dollars paid annually for acquiring emerging therapeutic companies can be seen in Chart 7. For R&D-stage emerging companies, 2011 remains the stand out year of the decade in dollar terms, due to the \$11 billion acquisition of Pharmasset, the largest Phase II deal in history. Save for that 2011 acquisition, 2014 is the biggest year in total dollars (\$9.6 billion) for R&D-stage buyouts in a decade. The increase in Phase III acquisitions was the notable driver for 2014, as were more multi-billion dollar upfronts paid for anti-viral companies. This drove the mean average price paid for a company to two times the average for the last five years, \$335 million vs \$665 million in 2014. For market-stage emerging companies, 2014 was actually a down year for acquisition volume and dollars.

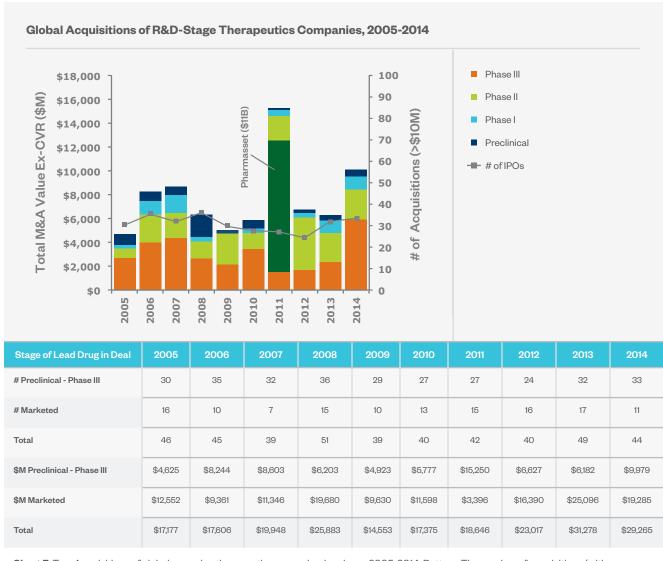


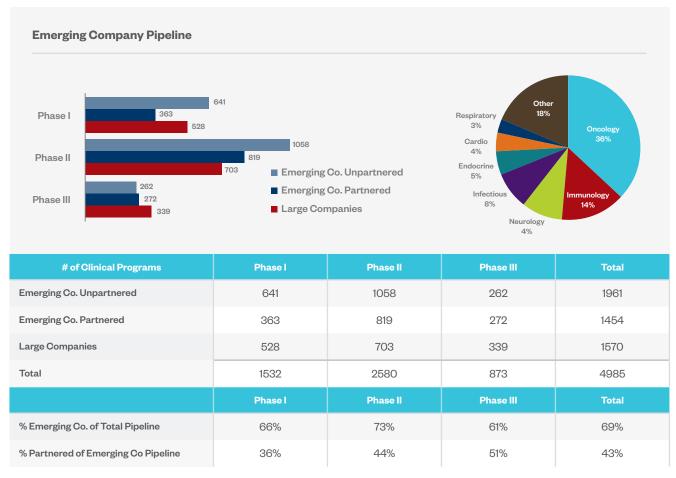
Chart 7. Top: Acquisitions of global emerging therapeutic companies, by phase, 2005-2014. Bottom: The number of acquisitions (with values above \$10M) and total dollars raised per year for R&D-stage and market-stage companies.

# **Clinical Pipeline**

Emerging companies have a robust pipeline, with over 3,400 drug indication programs under development, based on recent analysis of the BioMedTracker database. This accounts for a full 69% of the entire global industry pipeline.

Roughly 43% of these programs are partnered with other companies, demonstrating the importance of licensing and alliance development in the industry. Late-stage compounds are more likely to be partnered than early-stage assets. For example, only 36% of emerging company drug indication programs in Phase I are partnered, whereas 51% in Phase III are partnered.

Phase I, II, and III emerging company programs account for 29%, 55%, and 16% of the emerging company pipeline respectively. To an extent, the size of the pipeline is proportional to levels seen in capital and deal flow. For example, Oncology makes up the largest percentage of the pipeline and accounts for the highest level of funding in Venture Capital, IPOs, FOPOs, and the highest annual deal amounts. Neurology and Infectious Disease are the second and third most funded areas for investment and deals and account for the third and fourth most clinical programs.



**Chart 8**. Top: Number of clinical (Phase I, II, III) Drug/Indication programs emerging therapeutic companies (blue) and large drug developers (red). Bottom: Percentage of the entire clinical pipeline from small vs large.

## PART II:

# **Investments and Deals Trends** by Disease Area 2005-2014

| Overview - US Investment |    |
|--------------------------|----|
| Overview - Global Deals  | 13 |
| Oncology                 | 14 |
| Infectious Disease       | 16 |
| Neurology                | 18 |
| Psychiatry               | 20 |
| Endocrine                | 22 |
| Metabolic                | 24 |
| Cardiovascular           | 26 |
| Immunology               | 28 |
| Gastrointestinal         | 30 |
| Respiratory              | 32 |
| Hematology               | 34 |
| Ophthalmology            | 36 |
| Other                    | 38 |
| Platform                 | 40 |
| Rare Disease             | 4  |
| Discussion               | 42 |
| Methodology              | 44 |
| Appendix & References    | 47 |

# US Investment by Disease, 2005-2014

| US Investment (\$M)<br>2005-2014 | US Vent  | ure  | US IPO   |      | US FO    | PO   | Total    |      |
|----------------------------------|----------|------|----------|------|----------|------|----------|------|
| Oncology                         | \$9,296  | 24%  | \$2,976  | 23%  | \$12,024 | 29%  | \$24,296 | 26%  |
| Infectious Disease               | \$4,205  | 11%  | \$1,423  | 11%  | \$7,285  | 18%  | \$12,912 | 14%  |
| Neurology                        | \$4,079  | 11%  | \$1,252  | 10%  | \$4,601  | 11%  | \$9,931  | 11%  |
| Psychiatry                       | \$950    | 2%   | \$92     | 1%   | \$45     | 0%   | \$1,087  | 1%   |
| Endocrine                        | \$2,466  | 6%   | \$767    | 6%   | \$3,677  | 9%   | \$6,910  | 7%   |
| Metabolic                        | \$2,169  | 6%   | \$699    | 5%   | \$3,174  | 8%   | \$6,042  | 7%   |
| Cardiovascular                   | \$2,255  | 6%   | \$407    | 3%   | \$1,665  | 4%   | \$4,327  | 5%   |
| Immunology                       | \$1,666  | 4%   | \$670    | 5%   | \$1,596  | 4%   | \$3,932  | 4%   |
| Gastrointestinal                 | \$1,026  | 3%   | \$557    | 4%   | \$1,890  | 5%   | \$3,474  | 4%   |
| Hematology                       | \$1,187  | 3%   | \$1,626  | 12%  | \$1,343  | 3%   | \$4,156  | 5%   |
| Respiratory                      | \$1,168  | 3%   | \$262    | 2%   | \$1,157  | 3%   | \$2,586  | 3%   |
| Ophthamology                     | \$1,880  | 5%   | \$573    | 4%   | \$793    | 2%   | \$3,246  | 4%   |
| Other Diseases                   | \$2,929  | 8%   | \$1,551  | 12%  | \$1,520  | 4%   | \$6,000  | 7%   |
| Platform                         | \$3,109  | 8%   | \$217    | 2%   | \$32     | 0%   | \$3,359  | 4%   |
| Total                            | \$38,385 | 100% | \$13,072 | 100% | \$40,801 | 100% | \$92,259 | 100% |

Chart 9. Ten year totals for US venture funding, initial public offerings (IPOs), and follow-on offerings (FOPOs), by disease. The percentage indicates the proportion of total dollars raised. For FOPOs, the total dollars includes only transactions raising over \$10 million. (The categories are ordered top to bottom as they appear in Part II.)

## Note on the Analysis of US Emerging Therapeutics Company Investments

Although there is a continuum of investments outlined herein, there are two caveats when analyzing this aggregate multi-year data. First, there are bigger swings in the year by year analysis for investment vs deal making. This is due in part to a macroeconomic effect and in part to idiosyncrasies surrounding single company offerings. Thus, the path over a decade may be more relevant for identifying investment trends. Secondly, Private Investments in Public Equity (PIPEs), such as Registered Direct Offerings to a single investor, are not included in this post-IPO offering analysis. PIPE investments totaled \$12.7 billion, or 23% of the \$53 billion total post-IPO offerings. The analysis of FOPOs here is intended to capture the broad, public investment sentiment in the sector.

# Global Deals by Disease, 2005-2014

| Venture Dollars<br>Raised (\$M) | Licensi<br>R&D-Sta |      | Acquisit<br>R&D-St |      | Acquisit<br>Market-S |      | Tota      |      |
|---------------------------------|--------------------|------|--------------------|------|----------------------|------|-----------|------|
| Oncology                        | \$8,602            | 24%  | \$20,503           | 27%  | \$38,382             | 28%  | \$67,487  | 27%  |
| Infectious Disease              | \$3,463            | 10%  | \$27,521           | 36%  | \$6,459              | 5%   | \$37,443  | 15%  |
| Neurology                       | \$4,691            | 13%  | \$3,748            | 5%   | \$2,574              | 2%   | \$11,014  | 4%   |
| Psychiatry                      | \$969              | 3%   | \$255              | 0.3% | \$3,824              | 3%   | \$5,048   | 2%   |
| Endocrine                       | \$2,437            | 7%   | \$2,333            | 3%   | \$7,838              | 6%   | \$12,608  | 5%   |
| Metabolic                       | \$1,760            | 5%   | \$1,136            | 1%   | \$1,572              | 1%   | \$4,468   | 2%   |
| Cardiovascular                  | \$2,161            | 6%   | \$3,873            | 5%   | \$5,988              | 4%   | \$12,022  | 5%   |
| Immunology                      | \$2,560            | 7%   | \$4,054            | 5%   | \$14,221             | 10%  | \$20,834  | 8%   |
| Gastrointestinal                | \$1,571            | 4%   | \$1,813            | 2%   | \$7,252              | 5%   | \$10,636  | 4%   |
| Hematology                      | \$1,154            | 3%   | \$989              | 1%   | \$1,282              | 1%   | \$3,425   | 1%   |
| Respiratory                     | \$766              | 2%   | \$1,496            | 2%   | \$11,580             | 8%   | \$13,842  | 6%   |
| Ophthalmology                   | \$891              | 2%   | \$1,652            | 2%   | \$1,512              | 1%   | \$4,055   | 2%   |
| Other Diseases                  | \$2,027            | 6%   | \$2,723            | 4%   | \$35,850             | 26%  | \$40,600  | 16%  |
| Platform                        | \$2,813            | 8%   | \$4,317            | 6%   | \$0                  | 0%   | \$7,130   | 3%   |
| Total                           | \$35,865           | 100% | \$76,413           | 100% | \$138,334            | 100% | \$250,612 | 100% |

Chart 10. Ten year totals for R&D-stage licensing, R&D-stage acquisitions, and marketed product-stage acquisitions, by disease. 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 are included. (The categories are ordered top to bottom as they appear in Part II.)

## Note on the Analysis of Global Emerging Therapeutics Company Deals

With respect to licensing and acquisitions, there are two major differences between R&D-stage vs 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 and thus closely resemble licensing deals in structure. With respect to market-stage acquisitions, it should be noted that a number of companies that meet our definition of less than \$1 billion in sales fall into the "Specialty Pharma" area with multiple products on the market and no stand out lead product. They are thus grouped into the "Other" category.

# Oncology

| Oncology              | US Venture |     | US IPO  |     | US FOPO* |     | Global Licensing* |     | Global Acquisitions* |     |
|-----------------------|------------|-----|---------|-----|----------|-----|-------------------|-----|----------------------|-----|
| 2014#(%)              | 77         | 27% | 10      | 17% | 30       | 30% | 50                | 40% | 12                   | 27% |
| 2014 Amount \$M (%)   | \$1,199    | 26% | \$1,033 | 20% | \$2,090  | 24% | \$1,627           | 29% | \$1,435              | 5%  |
| 10 Year Total # (%)   | 642        | 22% | 40      | 23% | 163      | 31% | 324               | 25% | 101                  | 23% |
| 10 Year Total \$M (%) | \$9,296    | 24% | \$2,976 | 23% | \$12,024 | 29% | \$8,602           | 24% | \$58,885             | 27% |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

Oncology accounts for the largest percentage of funding in all five investment and deal categories. This may in part be due to the fact that the category itself is comprised of many different diseases. In fact, Oncology is often broken down into 100 different sub-indications in clinical trial databases, and the sub-indications are now being further differentiated at the molecular and cellular level. Such a highly differentiated set of diseases requires a broad range of investment interests to discover the right solutions for these unmet medical needs.

Venture Capital: Funding in Oncology continues to increase, with more than 90% of oncology venture investments going toward novel R&D as opposed to improvements of older regimens. Many of the investments over the last decade have led to innovative and promising advancements, such as immuno-oncology, targeted antibodies, and selective kinase inhibitors, where emerging companies have been at the forefront.

2014 was no exception, with the highest dollar amount for novel R&D funding in a decade. Much of the increase in R&D-stage funding went to Phase II-stage companies and companies working in the immuno-oncology field across all stages. For overall funding (novel R&D + Improvement R&D), 2014 was the second consecutive year of increase in dollars, jumping from \$1.0 billion in 2013 to \$1.2 billion in 2014. 2014 fell just short of the peak year in 2007.

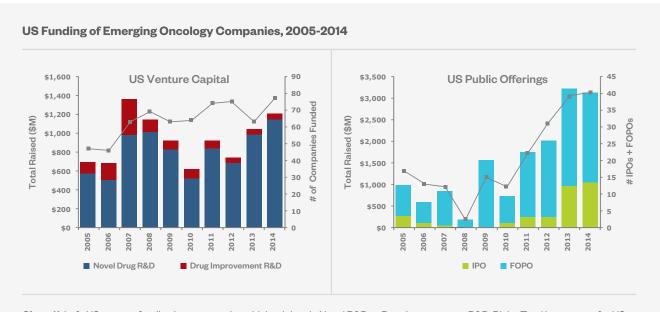


Chart 11. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: Oncology IPOs were strong in 2014, raising the most amount of capital (\$1.0 billion) compared to all other therapeutic categories and had the highest number of companies to go public (10). However, 2013 was even stronger, with a decade high of 18 IPOs, raising \$1.2 billion. Interestingly, 70% of 2014 oncology companies were early-stage companies (Preclinical/Phase I), which accounts for half of all the early-stage companies that went public last year.

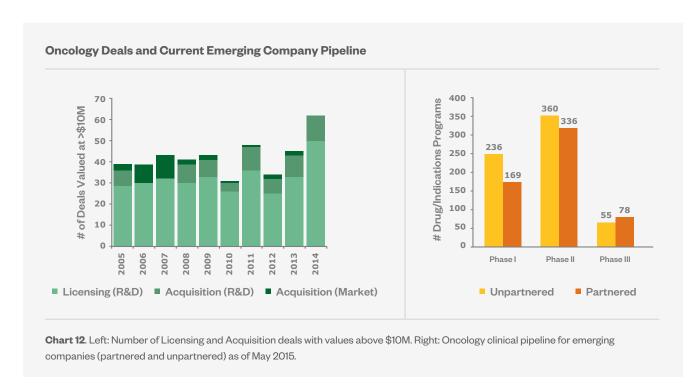
FOPOs: There were 30 Oncology FOPOs over \$10M in 2014, the most in a decade. For R&D-stage companies, 2014 was also a decade high in dollars raised (\$1,751 million). Over the last ten years, Oncology FOPOs numbered the highest in all but a single year, 2008, when two FOPOs were raised.

## Global Licensing and Acquisitions in Oncology

Licensing: There were 50 Oncology out-licensing deals in 2014 that had values above \$10 million. This is a significant increase representing 36% of the total number of deals in 2014 vs. an average of 26% of total number of deals each year since 2009. The continuing interest in immuno-oncology is driving this increase, accounting for much of the \$1.6 billion in 2014 upfront payments, the highest amount in a decade.

Acquisitions: The amount of 2014 upfront payments for Oncology R&D stage acquisitions was \$1.4 billion, a drop from the \$2 billion per year received during 2010-2013. Half of the 2014 upfront dollars were from a single \$725 million acquisition of a Phase I company. Many other acquisitions were below \$100 million in upfront value in 2014, placing the weight of the value contingent on milestones.

Pipeline: The emerging company clinical pipeline for Oncology is the largest of all the disease areas with 1,234 programs, and accounts for 67% of the total biopharmaceutical industry Oncology pipeline. This emerging company pipeline is heavily partnered, at 47%. More Phase III programs are partnered than not, with 78 Phase III programs being co-developed with partners, vs 55 independently pursued by small companies.



## Infectious Disease

| Infectious Disease    | US Venture |     | US IPO  |     | US FOPO* |     | Global Licensing* |     | Global Acquisitions* |     |
|-----------------------|------------|-----|---------|-----|----------|-----|-------------------|-----|----------------------|-----|
| 2014#(%)              | 33         | 11% | 8       | 13% | 10       | 10% | 11                | 9%  | 5                    | 11% |
| 2014 Amount \$M (%)   | \$528      | 11% | \$420   | 8%  | \$1,054  | 12% | \$196             | 3%  | \$6,502              | 22% |
| 10 Year Total # (%)   | 348        | 12% | 27      | 16% | 77       | 15% | 145               | 11% | 52                   | 12% |
| 10 Year Total \$M (%) | \$4,205    | 11% | \$1,423 | 11% | \$7,285  | 18% | \$3,463           | 10% | \$33,979             | 16% |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

Infectious diseases include viral, bacterial, fungal, and parasitic infections. There is high demand for novel drugs in these areas to reverse disease progression within patients and to stop wider spread throughout the population. The importance of novel drugs is of particular import in the antibiotic space where there has been a rise in strains resistant to older therapies. The vaccine space within Infectious Disease covers both viral and bacterial targets. Examples from the viral vaccine R&D front include new vaccines against influenza, SARS, RSV, HIV, and Ebola.

Venture Capital: In 2014, total venture funding for Infectious Disease surpassed \$500 million, a level not reached since 2007. With respect to phase of development for lead products, 2014 witnessed a resurgence in Phase II- and Phase III-stage company investment. Both 2013 and 2014 realized a 50% increase in total investment. Venture funding for R&D-stage Infectious Disease companies totaled \$4.1 billion over the last ten years, and accounted for 11% of total venture capital raised.

The largest amount of funding in 2014 went to companies with broad spectrum and gram-positive antimicrobials, with very little funding in gram-negative lead programs. Anti-fungal funding was the highest in a decade. Although HCV and HIV continue to drop in funding, other antiviral areas are strong. Vaccine funding (across all Infectious Diseases) was down in 2014 to the lowest level in six years.

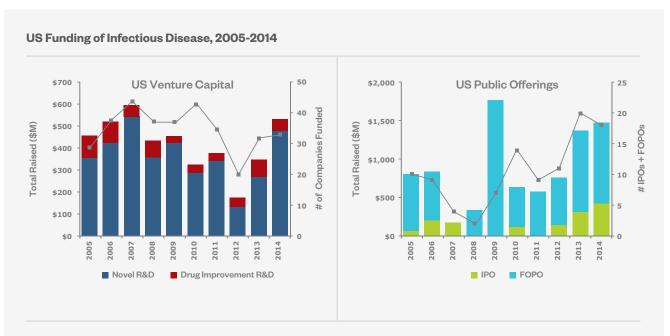


Chart 13. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: Over the last ten years 28 Infectious Disease companies have gone public, with 17 taking place in the last five years. 2014 was the biggest year in terms of the number of Infectious Disease companies with an IPO in the past decade, with eight companies. Infectious Disease is tied with the second largest disease group in terms of number of 2014 IPOs.

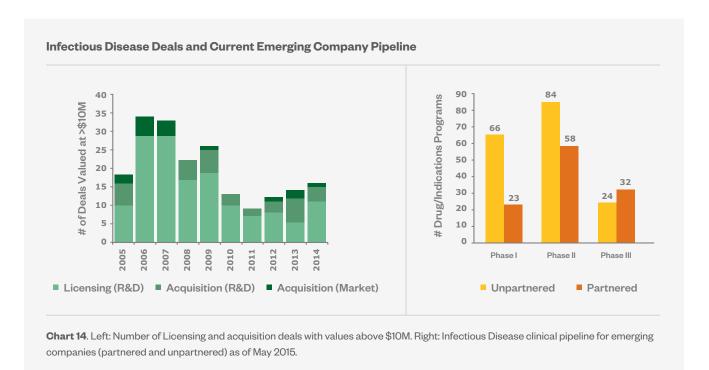
FOPOs: 2013 and 2014 both saw over \$1 billion raised by Infectious Disease company FOPOs, with 70% raised by R&D-stage companies. Outside of Oncology, the Infectious Disease category had the highest number of followons of the last decade (77) and raised the most capital (\$7.3 billion). Importantly, this was a highly diverse group of companies; although many were antiviral, most were outside the hepatitis C space and no single company has dominated the total amounts in recent years.

## Global Licensing and Acquisitions in Infectious Disease

Licensing: Although there were 11 out-licensing deals (with disclosed values of more than \$10 million) in 2014, the most since 2009, the dollar amount from upfronts (\$196 million) was below the average since 2009. Deals gaining the largest upfronts in 2014 were for Ebola (three deals) and pandemic influenza. Looking at the last ten years, there were twice as many deals per year from 2006-2009 vs the most recent four years.

Acquisitions: Two large acquisitions for R&D-stage antiviral-focused companies set 2014 apart from prior years, with upfronts of \$3.7 billion and \$1.6 billion. This helped propel Infectious Disease to the highest in total R&D-stage acquisitions dollars in ten years (\$27.5 billion in upfronts, Chart 10) compared to all other totals for disease areas. Over the same period, only 5% of market-stage acquisitions were attributable to Infectious Disease emerging companies.

Pipeline: The emerging company clinical pipeline for Infectious Disease contains 287 clinical programs. Half of this pipeline is in Phase II and almost half is partnered (41%) More Phase III programs are partnered vs. not partnered (32 of 56 programs, or 56%).



## Neurology

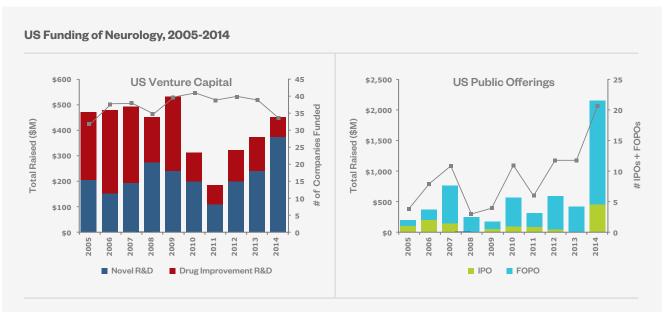
| Neurology             | US Venture |     | US IPO  |     | US FOPO* |     | Global Licensing* |     | Global Acquisitions* |     |
|-----------------------|------------|-----|---------|-----|----------|-----|-------------------|-----|----------------------|-----|
| 2014#(%)              | 34         | 12% | 8       | 13% | 13       | 13% | 11                | 9%  | 7                    | 16% |
| 2014 Amount \$M (%)   | \$453      | 10% | \$467   | 9%  | \$1,712  | 19% | \$586             | 10% | \$1,490              | 5%  |
| 10 Year Total # (%)   | 385        | 13% | 23      | 13% | 69       | 13% | 160               | 12% | 47                   | 11% |
| 10 Year Total \$M (%) | \$4,079    | 11% | \$1,252 | 10% | \$4,601  | 11% | \$4,691           | 13% | \$6,323              | 3%  |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

We split the Central Nervous System (CNS) diseases into two main groups: Neurology and Psychiatry. The area of Neurology includes neurodegenerative diseases such as Alzheimer's, Parkinson's, Amyotrophic lateral sclerosis (ALS), Huntington's disease, Multiple Sclerosis, brain and spinal cord disorders, sleep medicines, and the relatively large area of Pain. Psychiatry, analyzed later in this report, includes mental health disorders.

**Venture Capital:** Venture funding of companies with lead programs in Neurology increased for the third year in a row, to just over \$400 million in 2014, accounting for 12% of total venture capital raised by therapeutics companies. For novel drug R&D investment, 2014 was a decade high, and up 20% from 2013.

Parkinson's disease focused companies contributed to this increase with their biggest year in a decade, accounting for 25% of Neurology funding in 2014. Early-stage companies (Preclinical/Phase I) dominated the 2014 investment. Alzheimer's venture funding dropped 50% from 2013, and made up only 5% of the 2014 Neurology venture funding. Pain continued to be the most funded sub category, accounting for 30% of the Neurology funding in 2014. Over the last ten years, Pain has accounted for 42% of Neurology venture funding.



**Chart 15**. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: With seven companies completing an IPO in 2014, Neurology companies had the most IPOs this disease group has seen in a single year for the past decade. In fact, over the last ten years, only 17 Neurology companies have gone public, nine of them taking place in the last five years.

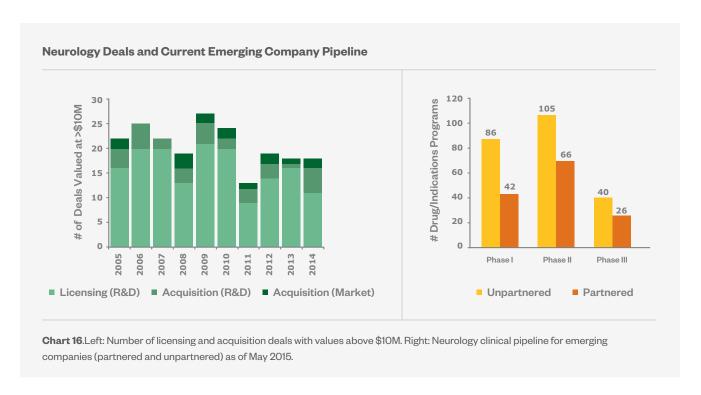
FOPOs: There was a 305% increase in follow-on dollars raised for Neurology emerging companies in 2014 vs. 2013, even though the number of companies funded increased by only one (12 vs 13). Over 75% of this went to R&D-stage companies. Neurology ranks third in total dollars raised in FOPOs over the last decade.

## Global Licensing and Acquisitions in Neurology

Licensing: There were 12 out-licensing deals in 2014 with disclosed values of more than \$10 million, a 25% drop from the sixteen deals per year on average since 2009. Although the deal number dropped, the total upfront payments were the highest since 2010. Interestingly, the bulk of the \$644 million in 2014 upfront payments came from very early (Preclinical) or very late-stage (Phase III) deals, in neurodegenerative diseases such as Alzheimer's, as well as Narcolepsy and Pain.

Acquisitions: 2014 was the biggest year in a decade in terms of the number of acquired emerging companies in Neurology (7) and total dollars paid upfront (\$1.5 billion). Two neurodegenerative disease focused companies accounted for the nearly 75% of the 2014 amount. Over the last decade, Neurology accounted for 10% of the total number of acquisitions, but only 3% of the total acquisition dollars over the last decade.

Pipeline: The emerging company clinical pipeline for Neurology contains 365 programs, the third highest of the major disease areas. Unlike the overall emerging company pipeline, Neurology has more unpartnered vs. partnered Phase III programs. Of the 66 Phase III programs, 40 (60%) remain unpartnered.



## **Psychiatry**

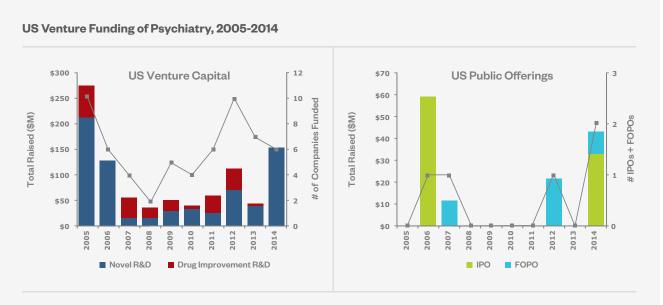
| Psychiatry            | US Venture |    | US IPO |    | US FOPO* |    | Global Licensing* |    | Global Acquisitions* |    |
|-----------------------|------------|----|--------|----|----------|----|-------------------|----|----------------------|----|
| 2014#(%)              | 6          | 2% | 1      | 2% | 1        | 1% | 1                 | 1% | 0                    | 0% |
| 2014 Amount \$M (%)   | \$154      | 3% | \$33   | 1% | \$11     | 0% | \$25              | 0% | \$0                  | 0% |
| 10 Year Total # (%)   | 60         | 2% | 2      | 1% | 3        | 1% | 28                | 2% | 6                    | 1% |
| 10 Year Total \$M (%) | \$950      | 2% | \$92   | 1% | \$45     | 0% | \$969             | 3% | \$4,079              | 2% |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

Psychiatric diseases include mental disorders such as Schizophrenia, Bipolar Disorder, PTSD, ADHD/ADD, OCD, Depression, Anxiety, and other mood related disorders.

**Venture capital:** Venture funding in Psychiatry reached a nine year high in 2014, to \$154 million, largely due to a single Phase II-stage company financing in the area of Depression. The number of companies in 2014 was at the ten year average of six. All six financings were for novel drugs.

A total of \$950 million has been raised since 2005, accounting for only 2% of the total \$38.5 billion raised by emerging therapeutic companies. That is five times less than Neurology. Average annual amounts raised for Depression and Schizophrenia, the largest sub-indications, are only \$41 million and \$21 million, respectively.



**Chart 17.** Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: Companies with a lead drug in the field of Psychiatry continue to be a rare sight on the IPO stage. However, 2014 turned out to be an exception as it had one company with an IPO that raised \$33 million. This is only one of two psychiatric companies that have completed an IPO in the past decade.

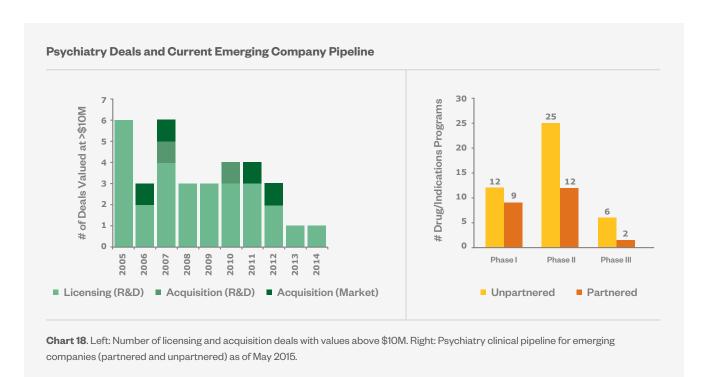
FOPOs: There were no follow-on offerings for companies with lead psychiatric drugs in 2014, and only a tiny amount raised from FOPOs over the last decade.

## Global Licensing and Acquisitions in Psychiatry

Licensing: Only a single deal (with disclosed value above \$10 million) was announced in each of the last two years. The total upfront amounts for Psychiatric disease deals has not surpassed \$250 million in any single year in the last decade, and in the last three years this has been below \$100 million.

Acquisitions: Only a single R&D-stage acquisition (of at least \$10 million in disclosed value) has been reported for a company with a lead drug in Psychiatry over the last decade. 2014 was no exception, making Psychiatry the lowest total upfront dollars for acquisitions in the last decade of the major disease categories. For emerging companies with marketed psychiatric drugs, there have been four acquisitions over the last decade, the last being in 2012.

Pipeline: The emerging company pipeline is thin for Psychiatry compared to Neurology, with 66 vs 365 programs, respectively. However, these 66 programs make up 60% of the entire industry's clinical pipeline. Psychiatry has a low percentage of partnered programs, with only 23 programs, or 34% of the pipeline partnered. There are only eight programs in Phase III and only two are partnered.



## **Endocrine Diseases**

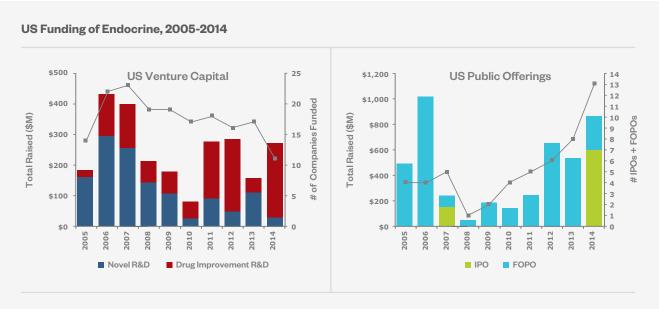
| Endocrine             | US Venture |    | US IPO |     | US FOPO* |    | Global Licensing* |    | Global Acquisitions* |    |
|-----------------------|------------|----|--------|-----|----------|----|-------------------|----|----------------------|----|
| 2014#(%)              | 11         | 4% | 8      | 13% | 5        | 5% | 7                 | 6% | 4                    | 9% |
| 2014 Amount \$M (%)   | \$272      | 6% | \$612  | 12% | \$255    | 3% | \$530             | 9% | \$137                | 0% |
| 10 Year Total # (%)   | 176        | 6% | 10     | 6%  | 42       | 8% | 77                | 6% | 21                   | 5% |
| 10 Year Total \$M (%) | \$2,466    | 6% | \$767  | 6%  | \$3,677  | 9% | \$2,437           | 7% | \$10,171             | 5% |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

The Endocrine Disease category contains Type I and II Diabetes, as well as hormone-related diseases including Osteoporosis, Acromegaly, Hypogonadism, Menopause, growth hormone deficiency. Type II Diabetes, on average, accounts for 40% of the funding in this category.

**Venture Capital:** In 2014, the number of companies being funded has plummeted to a decade low. In fact, only three companies working on new Endocrine drugs were funded in 2014. Novel R&D funding was only 11% of the total in Endocrine Diseases, as most of the funding in this space is for delivering already approved drugs.

Over the last decade, venture funding for Endocrine Diseases totaled \$2.46 billion, and accounted for 6% of total Venture capital raised. However, novel R&D funding accounts for only 39% of this total.



**Chart 19**. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: Endocrine companies, with 8 IPOs, tied with Infectious Disease companies for the second highest number of IPOs in 2014. However, Endocrine companies raised approximately \$200 million more capital, to \$612 million, making it the second highest amount among major disease groups. The majority of these IPOs were outside of Diabetes.

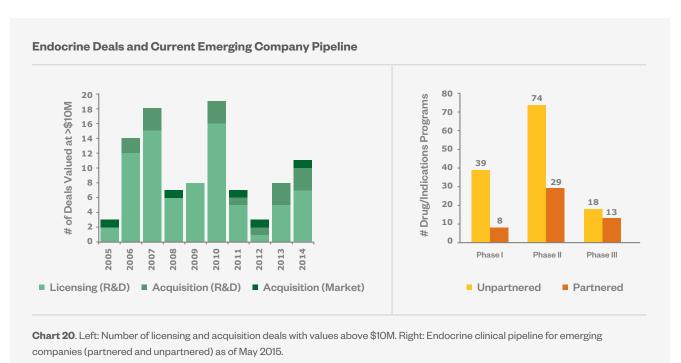
FOPOs: 2014 was a down year both in dollar terms and in number of FOPOs for Endocrine. The numbers from 2014 (5 deals for \$255 million) were levels not seen since 2011. Over the last decade, there have been 42 followon offerings totaling \$3.7 billion. More than two-thirds (29) were from R&D-stage companies. However, as most of these offerings were well under \$100 million, the market-stage company offerings account for half the overall amount raised in this category since 2005.

## Global Licensing and Acquisitions in Endocrine

Licensing: The seven deals in 2014 pushed the total upfront dollars close to a decade high (\$530 million). The number of deals in this space has increased over the last two years. Phase III deals for delivery or enhancement of existing products has dominated the Endocrine deal making space since 2005. This mirrors what has been seen in venture funding.

Acquisitions: 2014 was a down year in dollar terms, from \$730 million to \$130 million, but the number of deals remained about equal. For market-stage emerging Endocrine companies (with under \$1 billion in sales) there were five acquisitions over ten years accounting for \$7.8 billion, the majority of that for a single Diabetes company. There were 21 Endocrine company acquisitions over the last decade for a total of \$10.2 billion. R&D-stage companies accounted for 71% of these acquisitions (15 companies), but only 22% of the dollar value. Nine of those were for Diabetes-focused companies.

Pipeline: The emerging company pipeline has 181 active clinical programs, but is less partnered vs other disease areas. For example, only 28% of Phase II assets in Endocrine are partnered, vs. 44% for all disease areas.



## Metabolic Diseases

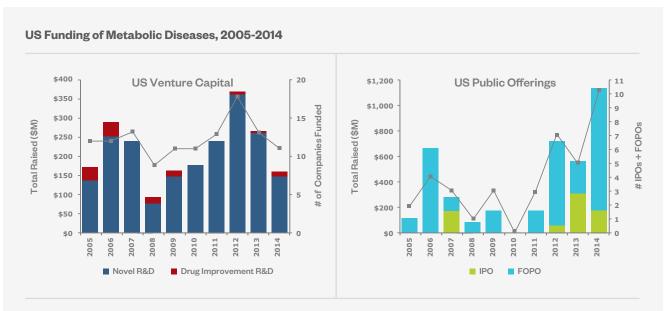
| Metabolic             | US Venture |    | US IPO |    | US FOPO* |     | Global Licensing* |     | Global Acquisitions* |    |
|-----------------------|------------|----|--------|----|----------|-----|-------------------|-----|----------------------|----|
| 2014 # (%)            | 11         | 4% | 2      | 3% | 8        | 8%  | 3                 | 2%  | 1                    | 2% |
| 2014 Amount \$M (%)   | \$161      | 3% | \$176  | 3% | \$949    | 11% | \$738             | 13% | \$89                 | 0% |
| 10 Year Total # (%)   | 123        | 4% | 8      | 5% | 30       | 6%  | 39                | 3%  | 10                   | 2% |
| 10 Year Total \$M (%) | \$2,169    | 6% | \$699  | 5% | \$3,174  | 8%  | \$1,760           | 5%  | \$2,708              | 1% |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

The Metabolic category covers a wide range of diseases, from rare genetic diseases to broader population diseases, such as obesity. This group also includes Cachexia, Familial Amyloid Polyneuropathy, Hyperkalemia, and other metabolic disorders.

**Venture Capital:** Venture funding for Metabolic Diseases for the last decade reached \$2.2 billion, or 6% of the total raised during that timeframe. The majority of investment in this space went toward novel R&D funding. Curiously, 2013 and 2014 were consecutive down years in a time of rising interest in developing drugs for genetic disorders. Some of this may be explained by the large peak in 2012 being influenced by just two rare disease companies raising B and D rounds prior to going public.

When comparing two five-year windows (2005 to 2009 vs. 2010 to 2014), Metabolic funding experienced the opposite trend of Endocrine. Novel R&D funding is up 50% for Metabolic and down 68% for Endocrine. This divergence can be explained by the sub-indications under each area. For Endocrine, a drop in Type II Diabetes funding of novel drug R&D was the culprit. For Metabolic, the rising interest in genetic diseases explains the increase. All of the funding for rare genetic disorders went into novel R&D.



**Chart 21**. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: 2014 was a modest year for Metabolic companies with only two companies completing an IPO, down from three in 2013. Between the two companies \$177 million was raised, with \$121 million going to a Phase II rare disease company. Over the past decade only eight metabolic companies have gone public, with six of them going public in the last five years.

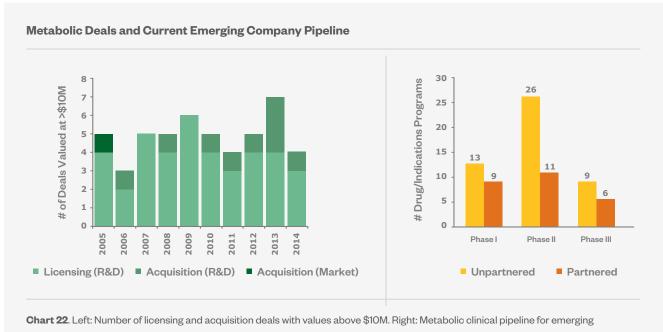
FOPOs: All of the 2013 and 2014 follow-on offerings were from rare disease companies, and the majority were for over \$100 million each. Prior to 2013, follow-ons in this category were dominated by Obesity drug developers.

#### Global Licensing and Acquisitions in Metabolic

Licensing: Only three deals (with potential values over \$10 million) fell into the Metabolic area in 2014. These three deals were for rare metabolic disorders and brought in \$738 million in upfront payments, the vast majority of which was for one company licensing multiple assets. The 10 year average is only \$176 million.

Acquisitions: 2014 was a down year in total dollars: \$89 million versus an average of \$200 million over the prior five years. For market-stage Metabolic companies, there has been only one acquisition (back in 2005). Although Metabolic R&D-stage companies accounted for just 1% of the total acquisition dollars, at \$1.1 billion over the last decade, most of this has come in recent years. Almost all of these nine acquisitions have been in the rare genetic disorder category.

Pipeline: The emerging company pipeline for Metabolic diseases has 74 active clinical programs. Like Endocrine, Metabolic has a far less partnered pipeline than the average for other disease areas. More than twice as many programs in Phase II are unpartnered vs partnered. Of the 15 programs in Phase III, six are partnered.



companies (partnered and unpartnered) as of May 2015.

## Cardiovascular

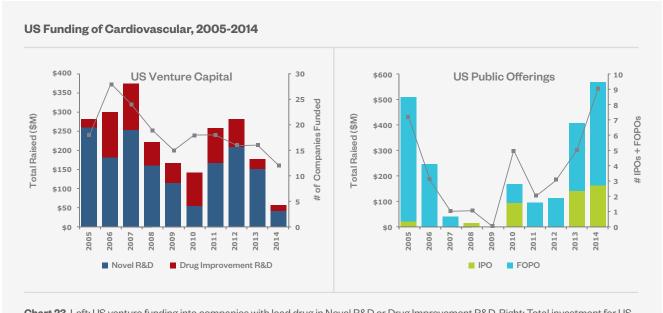
| Cardiovascular        | US Venture |    | US IPO |    | US FOPO* |    | Global Licensing* |    | Global Acquisitions* |    |
|-----------------------|------------|----|--------|----|----------|----|-------------------|----|----------------------|----|
| 2014 # (%)            | 12         | 4% | 3      | 5% | 6        | 6% | 4                 | 3% | 1                    | 2% |
| 2014 Amount \$M (%)   | \$56       | 1% | \$161  | 3% | \$345    | 4% | \$91              | 2% | \$42                 | 0% |
| 10 Year Total # (%)   | 184        | 6% | 9      | 5% | 27       | 5% | 59                | 5% | 21                   | 5% |
| 10 Year Total \$M (%) | \$2,255    | 6% | \$407  | 3% | \$1,665  | 4% | \$2,161           | 6% | \$9,861              | 5% |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

Cardiovascular includes indications such as Heart Failure, Acute Coronary Syndrome, Atherosclerosis, Hypercholesterolemia, and Hypertension.

**Venture Capital:** Similar in scale to Endocrine and Metabolic, Cardiovascular has received a total of \$2.5 billion in venture funding over the last ten years, and accounted for 6% of total venture capital raised. However, the funding has suffered the same fate as Endocrine. In fact, 2014 was the worst year in the decade in terms of both dollars and number of companies (only \$52 million to 12 companies).

Earlier in the decade, delivery and reformulations accounted for as much as 60% of the funding in Cardiovascular vs only 10-15% in recent years. Some of that funding has dried up, but the shift to more novel R&D funding fails to explain the sizable drop in2014. There does not appear to be a single sub-indication that accounts for the drop, although the "other" group that includes Heart Failure and Acute Coronary Syndrome, has dropped from \$257 million in 2012 to \$55 million in 2014 (see Appendix A2).



**Chart 23**. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: There were three cardiovascular companies that completed an IPO in 2014. That is one more company than 2013, and the highest number of companies to go public in this disease group in the past ten years.

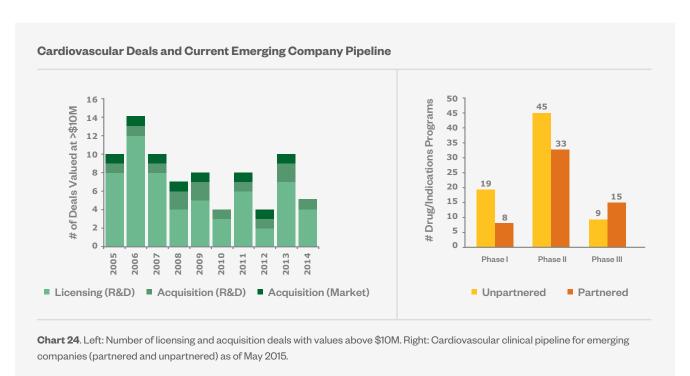
FOPOs: Cardiovascular follow-ons have seen a healthy, diverse revival for Phase II and III companies over the last two years. The dollars raised in 2014 for these R&D-stage company follow-ons is not large, at \$365 million, but neither is the Cardiovascular overall amount raised (\$1.06 billion in a decade for R&D-stage companies). From 2008 to 2012 only two companies in Cardiovascular had follow-ons.

#### Global Licensing and Acquisitions in Cardiovascular

Licensing: 2014 was a down year from 2013 in terms of the number of deals (from seven to four with disclosed value of more than \$10 million), but this is on par with the average for the previous five years. The \$91 million paid out in 2014 as upfront payments is only 2% of the total for emerging company out-licensing. Top deals include companies using cell-based approaches to heart disease and one small molecule approach targeting heart failure.

Acquisitions: There was only one Cardiovascular acquisition in 2014. However, the last ten years have only seen one or two acquisitions on average. Since 2005, Cardiovascular companies accounted for \$9.9 billion in acquisition dollars. R&D-stage Cardiovascular companies accounted for 40% (\$3.9 billion) of acquisition upfront dollars across thirteen companies. Nearly 90% of the dollars spent on acquisitions were spent in the early part of the decade (2005-2009).

Pipeline: A total of 129 clinical programs are being developed by small companies, and 43% of these are partnered. The Phase III pipeline is 62% partnered, higher than most other therapeutic areas.



# Immunology (non-GI, non-Respiratory)

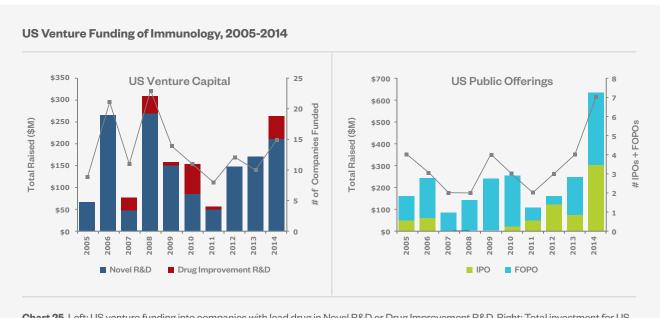
| Immunology            | US Venture |    | US IPO |    | US FOPO* |    | Global Licensing* |    | Global Acquisitions* |     |
|-----------------------|------------|----|--------|----|----------|----|-------------------|----|----------------------|-----|
| 2014#(%)              | 15         | 5% | 4      | 7% | 3        | 3% | 6                 | 5% | 3                    | 7%  |
| 2014 Amount \$M (%)   | \$262      | 6% | \$302  | 6% | \$334    | 4% | \$82              | 1% | \$6,243              | 21% |
| 10 Year Total # (%)   | 134        | 5% | 11     | 6% | 23       | 4% | 111               | 9% | 22                   | 5%  |
| 10 Year Total \$M (%) | \$1,666    | 4% | \$670  | 5% | \$1,596  | 4% | \$2,560           | 7% | \$18,275             | 9%  |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

Immunology covers a set of diseases that are primarily of autoimmune origin, such as Rheumatoid Arthritis and Psoriasis. For this section, we excluded immune-based diseases that are covered under the Gastrointestinal (e.g., Crohn's) and Respiratory (e.g., Asthma) sections below. This category also includes Graves' disease, Lupus, Primary Biliary Cirrhosis, Celiac Disease, Gout, and many other diseases. Immuno-oncology drugs in development fall under Oncology when the lead indication is oncology.

Venture Capital: 2014 venture investment increased to \$262 million, a five year high and across an above average 15 companies.

Total venture capital raised for Immunology was \$1.6 billion for the ten-year period, or 4% of the total venture capital raised. Investment has been rising since 2012, and 2014 was the highest year since 2008. The majority of investment in this space is for early-stage (Preclinical/Phase I) companies working on novel therapeutics.



IPOs: More than a third of the \$302 million raised by four Inflammation focused companies that went public in 2014 was from a single company marketing a Rheumatoid Arthritis drug. There have been 11 Inflammation company IPOs over the past ten years, and two-thirds of them took place in the past five years.

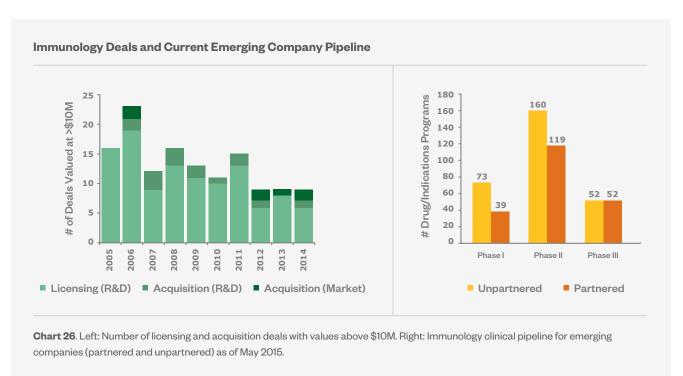
FOPOs: There were three FOPOs in 2014 from Immunology companies raising \$334 million. Most of the activity over the last ten years in Immunology follow-ons comes from Phase III companies, not market-stage companies. Furthermore, the majority of the follow-on dollars raised in this category came from just three companies over the last few years, with one raising \$258 million over two years for a Phase III product.

## Global Licensing and Acquisitions in Immunology

Licensing: The last few years (2012-2014) have seen a drop in licensing activity for immunology focused deals compared to the 2005 to 2010 period. The drop in 2014 made last year the second lowest in both upfront totals and deal number (for deals above \$10 million) in a decade. Some immune system based companies have been striking deals in the immuno-oncology space recently, which applies the technologies and targets of immunology research toward cancer cells. The top deal was for small molecule antagonists of new enzyme targets, the other top deals were for antibody therapies in various autoimmune indications.

Acquisitions: Three Immunology acquisitions totaling \$6.2 billion took place in 2014. Although this was above average in dollar terms, the majority went to a single market-stage company. Looking at the last decade, there has been a surge in acquisitions for market-stage emerging immunology companies in the last three years with five deals totaling almost \$13 billion. R&D-stage Immunology acquisitions, averaging one or two per year, have accounted for \$4 billion since 2005.

Pipeline: The Immunology clinical pipeline is the second largest for emerging companies, with 495 programs. Partnering from earlier years has led to half of all Phase III programs (52 each) being partnered and 45% of Phase II programs (119 of 260) are partnered.



## Gastrointestinal Diseases

| Gastrointestinal      | US Venture |    | US IPO |    | US FOPO* |    | Global Licensing* |     | Global Acquisitions* |     |
|-----------------------|------------|----|--------|----|----------|----|-------------------|-----|----------------------|-----|
| 2014#(%)              | 4          | 1% | 1      | 2% | 3        | 3% | 5                 | 4%  | 2                    | 5%  |
| 2014 Amount \$M (%)   | \$18       | 0% | \$60   | 1% | \$345    | 4% | \$758             | 13% | \$3,927              | 13% |
| 10 Year Total # (%)   | 66         | 2% | 8      | 5% | 23       | 4% | 7                 | 2%  | 13                   | 3%  |
| 10 Year Total \$M (%) | \$1,026    | 3% | \$557  | 4% | \$1,890  | 5% | \$1,571           | 4%  | \$9,065              | 4%  |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

The majority of the Gastrointestinal Diseases category is split into two main sub-disease areas: Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD), but there are many other diseases that fit into this area. The main types of IBD are Crohn's disease and Ulcerative Colitis (UC), and these are often categorized by database providers under immunology, not Gl. IBS is a non-inflammatory chronic condition affecting the large intestine. Other areas include Gastroenterological disorders, Chronic Idiopathic Constipation, Ulcers, Dyspepsia, Gastroparesis, Exocrine Pancreatic Insufficiency, Liver failure/Cirrhosis, Colon Cleansing/Laxatives, and other Gl disorders.

**Venture Capital:** There has been a collapse of venture funding for Gastrointestinal Diseases, similar in severity to Endocrine and Cardiovascular. 2014 was the worst year on record in dollar terms, with just \$18 million attributed to companies with lead Gastrointestinal products. Over the last five years, \$290 million has been raised, a drop of 61% from \$731 million over the previous five years.

Both IBD and IBS show a collapse in novel drug R&D funding, with essentially no funding of novel R&D for IBD in 2014.

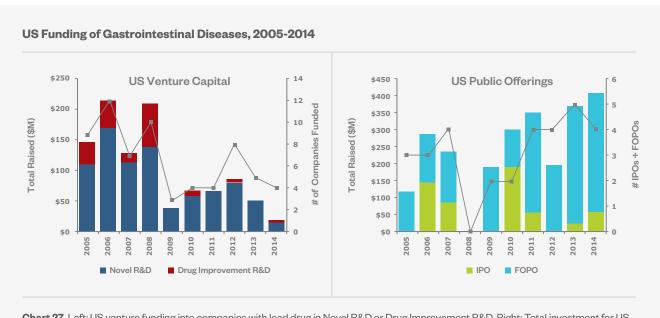


Chart 27. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: In 2014 there was only one company with a lead drug in the Gastrointestinal field that completed an IPO. Over the past decade there have only been seven R&D-stage companies that have completed an IPO in this therapeutics category with four of them taking place in the past five years. All seven of the companies were in the later stages of development (Phase II or III).

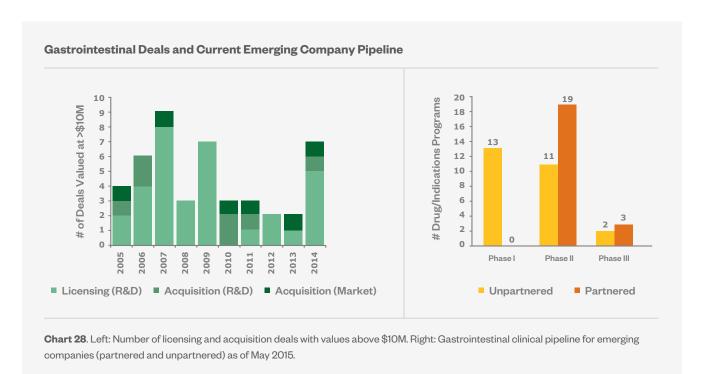
FOPOs: 2014 was very similar to 2013: three deals raised \$345 in 2014 vs. four deals totaling \$342 in 2013. These are the two strongest years of the decade. The majority of the dollars raised in both years were by market-stage companies. This contrasts with the first part of the last decade when the opposite was true - all follow-ons in this category were Phase II or Phase III.

#### Global Licensing and Acquisitions in Gastrointestinal

Licensing: 2014 was a big year for Gastrointestinal deal making. There were five deals with potential value of more than \$10 million, which is far above the one or two per year since 2011. Aggregate upfront payments reached a decade high, in large part due to the largest upfront in history (\$710 million for an asset with a completed Phase II trial).

Acquisitions: 2014 was the biggest year in terms of both numbers and total dollars from Gastrointestinal acquisitions. Similar to what was found with Immunology, a lot of the recent acquisition activity for emerging Gastrointestinal has been for market-stage companies. These acquisitions have averaged less than one per year, but they account for most of the dollars over the last decade - \$7.3 billion vs \$1.8 billion for R&D-stage companies.

Pipeline: The Gastrointestinal pipeline is rather small compared to other major disease areas, with just 48 programs. However, the Gastrointestinal space is heavily partnered, more so than any other disease area: 63% of Phase II programs are partnered, and 66% of Phase III programs (2 of the 5).



# Hematology (non-oncology)

| Hematology            | US Venture |    | US IPO  |     | US FOPO* |    | Global Licensing* |    | Global Acquisitions* |    |
|-----------------------|------------|----|---------|-----|----------|----|-------------------|----|----------------------|----|
| 2014 # (%)            | 5          | 2% | 3       | 5%  | 5        | 5% | 4                 | 3% | 1                    | 2% |
| 2014 Amount \$M (%)   | \$47       | 1% | \$309   | 6%  | \$403    | 5% | \$260             | 5% | \$70                 | 0% |
| 10 Year Total # (%)   | 80         | 3% | 10      | 6%  | 20       | 4% | 41                | 3% | 8                    | 2% |
| 10 Year Total \$M (%) | \$1,187    | 3% | \$1,626 | 12% | \$1,343  | 3% | \$1,154           | 3% | \$2,271              | 1% |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

The Hematology category includes Blood Stimulators, Coagulation agents, Anemia, Antithrombotic, Chronic Venous Ulcers, Peripheral Arterial Disease (PAD), Sickle Cell Disease, Iron Overload, Hemophilia, and Neutropenia/ Leukopenia. Some of these diseases are rare, and therefore are also analyzed in the rare disease section of this report.

Venture Capital: Funding for Hematology has declined to the lowest level in a decade, both in dollar terms and number of companies (five companies and \$47 million). This compares to peak years of 2005, 2007, and 2012 when more than \$150 million per year went into this area. However, those peak years can be explained by just a few companies accounting for the majority of the annual investments.

Almost half of the investment before 2009 was for blood stimulators. Coagulation accounted for most of the 2014 venture capital in this area. Areas outside blood stimulators and coagulation, which had been showing some increase in the last few years, dropped to almost zero in 2014.

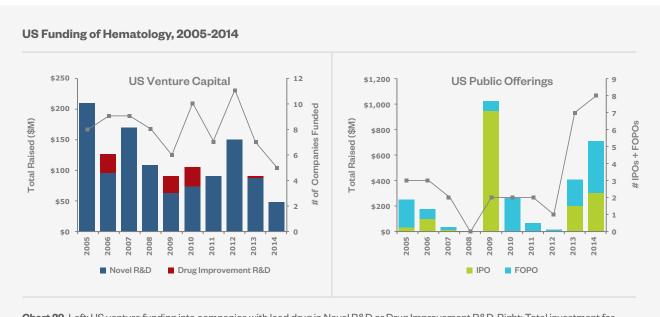


Chart 29. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: In 2013 and 2014 we saw a resurgence of Hematology companies in the IPO market with three companies going public each year. Over the past decade there have been eight development-stage Hematology companies that have completed an IPO. All six from the past two years were in Phase II or Phase III development.

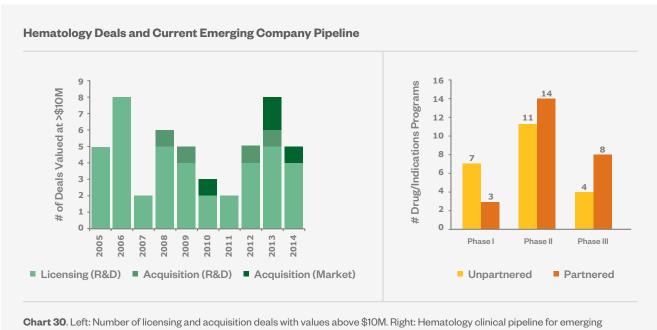
FOPOs: All emerging company follow-ons in Hematology since 2010 have been from R&D-stage companies. 2014 was the highest # in a decade for Hematology largely due to one Phase II and one Phase III FOPO.

## Global Licensing and Acquisitions in Hematology

Licensing: 2014 was a strong year for Hematology with four deals (valued over \$10 million) covering cell and gene therapies, mainly for rare blood disorders and hemophilia.

Acquisitions: The five R&D-stage acquisitions in Hematology, totaling \$980 million, accounted for just 1% of the total R&D-stage acquisitions over the last decade. Half the years, including 2014, do not contain a single transaction disclosed with over \$10 million in value. For market-stage emerging companies, there were only four deals in the last ten years.

Pipeline: With 47 programs, the Hematology clinical pipeline for emerging companies is the same size as the Gastrointestinal pipeline and the smallest of all major disease areas. However, partnering is a core component in Hematology R&D, with Phase II and III programs partnered at 56% and 67%, respectively.



companies (partnered and unpartnered) as of May 2015.

## **Respiratory Diseases**

| Respiratory           | US Venture |    | US IPO |    | US FOPO* |    | Global Licensing* |    | Global Acquisitions* |     |
|-----------------------|------------|----|--------|----|----------|----|-------------------|----|----------------------|-----|
| 2014 # (%)            | 6          | 2% | 0      | 0% | 3        | 3% | 3                 | 2% | 1                    | 2%  |
| 2014 Amount \$M (%)   | \$49       | 2% | \$0    | 0% | \$432    | 5% | \$57              | 1% | \$8,015              | 27% |
| 10 Year Total # (%)   | 98         | 3% | 3      | 2% | 12       | 2% | 38                | 3% | 14                   | 3%  |
| 10 Year Total \$M (%) | \$1,168    | 3% | \$262  | 2% | \$1,157  | 3% | \$766             | 2% | \$13,076             | 6%  |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

Respiratory diseases examined include a number of common diseases such as Asthma, COPD, and Idiopathic Pulmonary Fibrosis (IPF), as well as other diseases such as Cystic Fibrosis, Emphysema, Acute Respiratory Failure, Acute Lung Injury (ALI), Acute Respiratory Distress Syndrome (ARDS), and other respiratory diseases.

**Venture Capital:** 2014 reached a new decade low for companies with lead programs in Respiratory disease, both in dollar terms and in number of companies financed. Of the \$49 million raised in 2014, most went to a single Phase II Asthma company.

Total venture capital raised for Respiratory Diseases was \$1.1 billion for the ten-year period, or 3% of the total venture capital raised for therapeutics. Funding has dropped significantly over the years, from over \$200 million at the 2007 peak for fourteen companies, to under \$50 million to just six companies in 2014. Looking at specific indications, COPD was one of the few respiratory areas that was increasing post-2008, but no lead product COPD companies were recorded for 2014. Most companies pursuing multiple lead therapies in multiple respiratory areas in years prior to 2013 were found to be delivery companies.

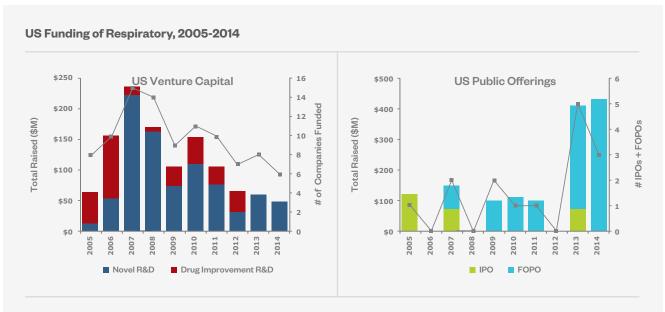


Chart 31. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: Respiratory companies saw only three IPOs in the last decade, the second fewest of all disease groups. The most recent IPO of a R&D-stage respiratory company was in 2013 with the remaining two taking place in 2005 and 2007.

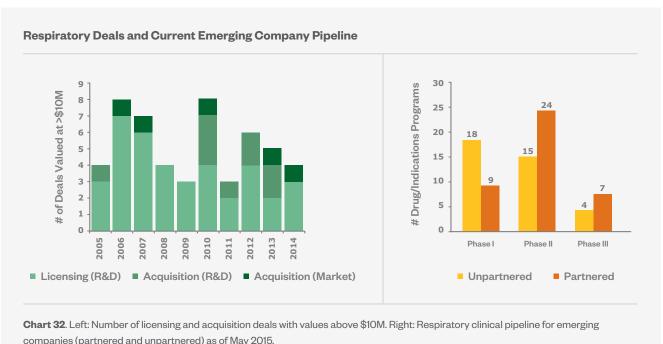
FOPOs: There were three Respiratory company FOPOs raising \$432 million in 2014. Although there has been an increase in recent years, 67% of the follow-on dollars raised in the Respiratory category came from just three market-stage companies. For R&D-stage Respiratory companies, only five follow-ons have been seen in the last ten years, raising \$290 million.

### Global Licensing and Acquisitions in Respiratory

Licensing: 2014 had three quite varied deals: The largest upfront was for lung transplant, the other two covered for COPD, asthma, and idiopathic pulmonary fibrosis (IPF). Respiratory licensing deals have averaged roughly three deals per year since 2005.

Acquisitions: For market-stage companies, 2014 produced one of the biggest Respiratory acquisitions of the decade. Although there was not a single R&D-stage acquisition in 2014, there has also been an increase in R&Dstage acquisitions during the 2010-2013 time frame. For this four year period there were eight acquisitions vs. none for the prior four years. Most of the nine R&D-stage companies focused primarily on COPD and Asthma.

Pipeline: The Respiratory clinical pipeline has 77 programs. The Phase II/Phase III pipeline is heavily partnered compared with other diseases, with 61% of programs partnered.



companies (partnered and unpartnered) as of May 2015.

## Ophthalmology

| Ophthalmology         | US Venture |    | US IPO |    | US FOPO* |    | Global Li | censing* | Global Acquisitions* |    |  |
|-----------------------|------------|----|--------|----|----------|----|-----------|----------|----------------------|----|--|
| 2014#(%)              | 15         | 5% | 4      | 7% | 4        | 4% | 4         | 3%       | 2                    | 5% |  |
| 2014 Amount \$M (%)   | \$293      | 4% | \$267  | 5% | \$284    | 3% | \$418     | 7%       | \$67                 | 0% |  |
| 10 Year Total # (%)   | 145        | 5% | 7      | 4% | 15       | 3% | 31        | 2%       | 13                   | 3% |  |
| 10 Year Total \$M (%) | \$1,880    | 5% | \$573  | 4% | \$793    | 2% | \$891     | 2%       | \$3,164              | 1% |  |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

Many of the companies with lead programs in the Ophthalmology space work on macular degeneration but with new biologics platform technologies, such as gene therapy or novel target binding proteins (non-antibody scaffolds).

**Venture Capital:** Ophthalmology reached a decade high in 2014, with \$293 million raised. Although the average number of companies receiving funds per year has increased over time, 2014 was a down year compared to 2013. In 2014, early-stage investments were scarce compared to Phase II and Phase III stage company investments.

Ophthalmology venture funding totaled \$1.88 billion over the last decade, representing 5% of the total venture capital raised. Year-to-year totals are choppy, but investment interest has maintained the \$250 million-plus level for the last two years, the highest consecutive years in a decade. A high degree of novel R&D has been funded over the last decade, as can be seen in Chart 33.

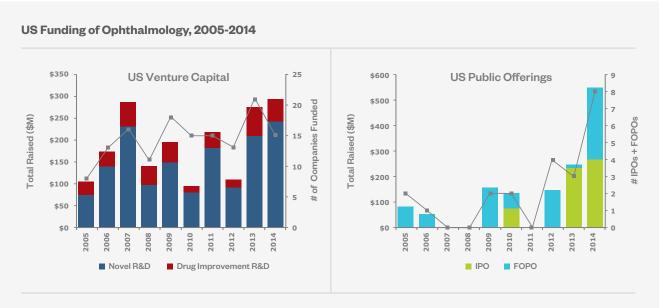


Chart 33. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: Over the past decade six development-stage Ophthalmology companies have completed an IPO, all of them taking place in the past five years. There were four Ophthalmology IPOs In 2014 alone, raising \$267 million.

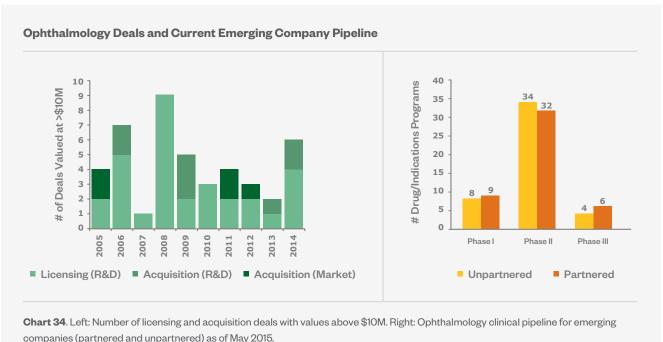
FOPOs: 2014 was the highest year in a decade in terms of the number of Ophthalmology FOPOs, with three R&D-stage companies and one market-stage company raising funds. The total raised was \$284, with \$115 million attributed to one market-stage company. Much of the \$793 million raised by Ophthalmology companies over the last ten years came in the last few years.

#### Global Licensing and Acquisitions in Ophthalmology

Licensing: The 2014 deal activity shows that Ophthalmology continues to be an area of increased interest for large companies. There were four deals (with over \$10 million in disclosed value) and \$418 million in upfront payments in 2014, the highest dollar amount in three years.

Acquisitions: There have been seven R&D-stage acquisitions in the last decade, but the upfront payments only total \$500 million, or 1% of the total acquisition upfronts. This places the upfronts below \$100 million on average per deal. For market-stage companies, five deals totaling \$1.5 billion have occurred over the last decade.

Pipeline: The Ophthalmology pipeline consists of 93 clinical programs, with 70% of them in Phase II trials. Half of the Phase II programs are partnered and more than half of Phase III programs are partnered. This is the only area with more Phase I programs partnered vs. unpartnered. Novel approaches such as gene therapy, aptamers, and new antibody targets are being co-developed.



companies (partnered and unpartnered) as of May 2015.

### Other Diseases

| Other Diseases        | US Venture |     | US IPO  |     | US FOPO* |    | Global Li | censing* | Global Acquisitions* |     |  |
|-----------------------|------------|-----|---------|-----|----------|----|-----------|----------|----------------------|-----|--|
| 2014 # (%)            | 25         | 9%  | 6       | 10% | 8        | 8% | 12        | 10%      | 2                    | 5%  |  |
| 2014 Amount \$M (%)   | \$321      | 19% | \$1,212 | 24% | \$646    | 7% | \$152     | 3%       | \$1,075              | 4%  |  |
| 10 Year Total # (%)   | 250        | 8%  | 11      | 6%  | 26       | 5% | 102       | 8%       | 63                   | 14% |  |
| 10 Year Total \$M (%) | \$2,929    | 8%  | \$1,551 | 12% | \$1,520  | 4% | \$2,027   | 6%       | \$38,572             | 18% |  |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

Many other diseases were funded that did not fit within our top 14 categories discussed above. These include Dermatology, Allergy, Musculoskeletal diseases, Osteoarthritis, Otology (ear diseases), Periodontitis, Urology, nonviral liver diseases, fertility drugs, and treatments for side-effects of chemotherapy or radiation.

Venture Capital: In aggregate, the funding for these diseases accounted for less than 10% of the total for any given year. More than 40% of funding in the "Other" group of diseases was split between Dermatology and Renal, with Dermatology accounting for the majority of the delivery development in the form of topical cream formulations of existing drugs.

2014 venture capital raised in this "other" disease category totaled \$321 million, roughly where the average has been across the last decade.

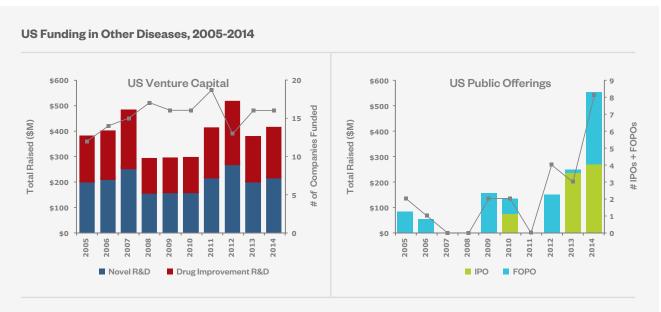


Chart 35. Left: US venture funding into companies with lead drug in Novel R&D or Drug Improvement R&D. Right: Total investment for US IPOs and US FOPOs per year, 2005-2014.

IPOs: For all of the other therapeutics categories, five R&D-stage IPOs took place in 2014. Those five IPOs account for the majority of the seven IPOs seen in the past decade, raising \$341 million.

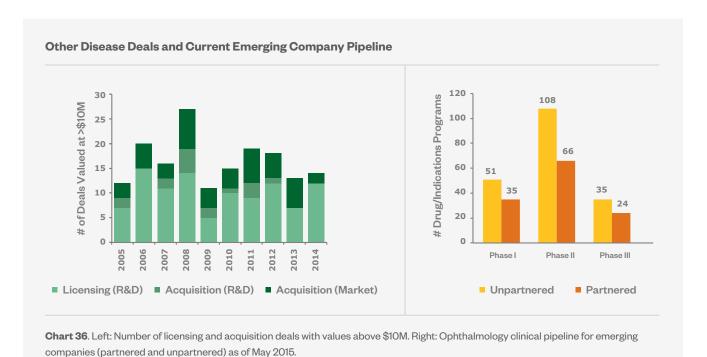
FOPOs: 2014 reached a decade high in both dollars raised (\$646 million) and number of companies (8) with FOPOs priced at over \$10 million. A large portion (80%) of the 2014 dollars went to R&D-stage companies in areas such as renal disease, fertility, aesthetic products, and rare disorders. 2013 was also a strong year, with \$418 million raised. All previous years were under \$150 million.

#### Global Licensing and Acquisitions in Other Diseases

Licensing: Although the \$2 billion in upfronts implies \$200 million per year on average, most years either fall short or greatly surpass this number. For example, 2010 saw a decade high with \$680 in upfront payments from licensing deals, followed by only \$98 million the following year. 2014 was closer to the average, at \$152 million, and was a solid increase from the \$95 million of 2013.

Acquisitions: This category contains more market-stage emerging company acquisitions (47) than R&D-stage acquisitions (16). A number of the companies were small specialty pharmaceuticals companies. The ten-year total spent on these small market-stage companies was \$35.8 billion, compared to just \$2.7 billion for R&D companies working in various areas.

Pipeline: The Other disease category contains 319 programs spread over many different indications outside the 12 main disease categories. More than half of these are in Phase II trials. Of the 174 Phase II programs in development only 36% are partnered. For Phase III, this percentage rises only slightly, to 41% (24 of 59).



### **Platform**

| Platform              | US Venture |     | US IPO |    | US FOPO* |    | Global Li | censing* | Global Acquisitions* |     |  |
|-----------------------|------------|-----|--------|----|----------|----|-----------|----------|----------------------|-----|--|
| 2014 # (%)            | 34         | 12% | 2      | 3% | 0        | 0% | 5         | 4%       | 3                    | 7%  |  |
| 2014 Amount \$M (%)   | \$868      | 3%  | \$102  | 2% | \$0      | 0% | \$142     | 3%       | \$175                | 1%  |  |
| 10 Year Total # (%)   | 276        | 9%  | 4      | 2% | 1        | 0% | 115       | 9%       | 44                   | 10% |  |
| 10 Year Total \$M (%) | \$3,109    | 8%  | \$217  | 2% | \$32     | 0% | \$2,813   | 8%       | \$4,317              | 2%  |  |

Licensing and acquisition totals include upfront payments only. The percentage indicates the proportion of total deals or total dollars raised. \*Includes only transactions valued over \$10M.

The Platform category contains primarily preclinical-stage companies that have a core technology in creating a diverse set of new molecules. Once companies identify a lead product and utilize the majority of their funds for that product, they are relabeled as a product company within a specific disease indication.

**Venture Capital:** 2014 was a record year for Platform companies, with \$868 million raised. A few companies involved with new RNA-based platforms accounted for half of this surge. On average, 25 companies per year received financing in this group, placing it near the top in both dollars raised and companies receiving investment.

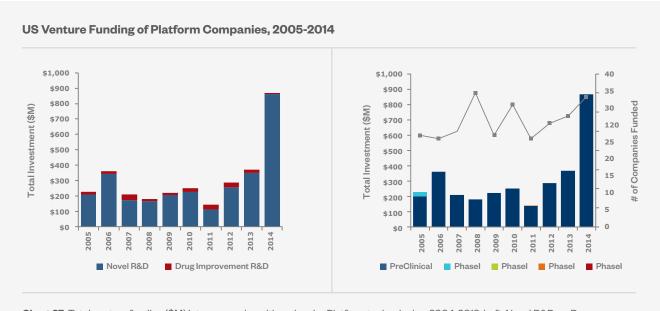


Chart 37. Total venture funding (\$M) into companies with molecular Platform technologies, 2004-2013. Left: Novel R&D vs. Drug Improvement R&D. Right: Total Investment by Phase of R&D.

**IPOs & FOPOs:** Only four IPOs and one FOPO for Platform companies have taken place since 2005. There are not many public companies without a lead program in a specific disease. Thus the low representation here is more of a reflection of the method of tagging deals.

**Licensing and Acquisitions:** There were 15 licensing deals with values above \$10 million in 2014, near the average of the decade. Looking at the last decade, this category made up 8% of all licensing deal upfront payments. To qualify, the deal terms must have broad potential, so many platform technologies in this report have been categorized into the disease for which they were licensed. For R&D-stage acquisitions, Platform was the third highest category in terms of dollars and in number of companies, for 2005-2014.

### Rare Disease

According to a recent report, there are 7,000 rare diseases that cumulatively affect 30 million Americans.<sup>6</sup> Only 350 therapeutics are approved for these diseases, indicating that thousands of rare diseases are without a treatment or cure.

Over the last ten years, there has been an increase in investment into rare diseases, with the highest amounts (over \$500 million per year) seen in 2012-2014. As shown below, most funding is directed to clinical trial-stage companies, with the exception of 2013 when nearly half of the funding went into Preclinical-stage companies.

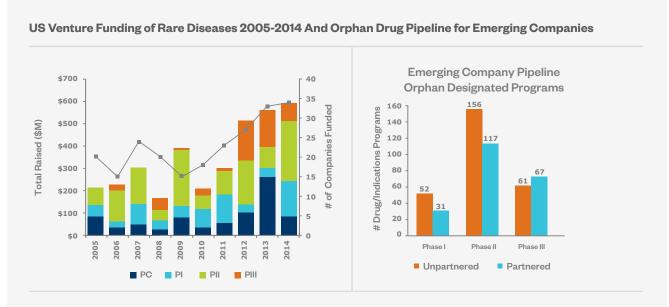


Chart 38. Left: Total venture funding (\$M) into companies with a lead drug in a rare disease, 2004-2013. Total Investment by Phase of R&D and Number of companies receiving financing per year for a specific venture round. Right: Clinical pipeline for Orphan Designated products developed by emerging companies (partnered and unpartnered) as of May 2015. (Note that 44% of all Orphan drugs in development are in Oncology).

IPOs & FOPOs: Many recent IPOs and FOPOs are from companies pursuing therapies for rare diseases, such as Duchenne Muscular Dystrophy and Childhood Cerebral Adrenoleukodystrophy. Of the fourteen IPOs from R&Dstage companies targeting a rare disease, all but two of the companies completed their IPO in the past three years. Six companies in 2014 raised a total of \$508 million from their IPOs. The two largest IPOs were both metabolicfocused companies and took place in 2013 and 2014, raising \$125 million and \$121 million respectively.

Licensing and Acquisitions: Increases in licensing and acquisitions have also been seen over the last few years. For example, the total number of rare disease acquisitions between 2010 -2014 (26) is up 74% from 2005 -2009 (15). Most of these tend to be R&D-stage companies developing products for rare, inherited disorders.

The pipeline for Orphan designated products developed by emerging companies contains 484 clinical programs, with 56% in Phase II and 26% in Phase III. Overall, 44% of this pipeline is partnered.

## Discussion

The aim of this study was to accurately define the levels of funding and deal interest for emerging therapeutic companies, and to do this by both stage of development and disease area. Analyzing trends over time and across therapeutic areas allows for the identification of strengths and weaknesses across this often fragile ecosystem of drug innovation.

In our previous report on venture capital for the years 2004 through 2013, we divided the ten year period into two halves, which allowed us to look at investment for the five years before the financial crisis of late 2008 versus the five years after. 7 What we found was that most disease areas with large populations have seen significant declines in novel R&D investment (ranging from 30% to 60% declines). Splitting up the most recent ten year period into two five year windows (2005-09 and 2010-14), reveals similar results, with two notable changes. Novel Neurology R&D venture investment jumped from a -39% drop (2004-08 vs 2009-13) to a +5% gain (2005-09 vs.2010-14). Contributing to this increase was a continued investment in pain and a rise in investment into Parkinson's Disease-focused companies in 2014. However, investment into Alzheimer's decreased more than 50% in 2014. Platform investment increased from +5% to +60%. There remains a split between haves and have-nots with respect to venture investment in disease areas. Cardiovascular, Respiratory, Gastrointestinal, and Endocrine are all down over 30% for the five year period comparison, while Ophthalmology, Metabolic (primarily rare disease), and Platform are up more than 10%.

The number of new companies receiving Series A financing is still down from peak levels, and in a big year for funding like 2014, we actually saw the dollars for Series A rounds decrease as well as the number of first time Series A financings. This is a trend we hope to see reversed with the increased access to capital in public markets observed in 2013 and 2014. The rejuvenation of the public markets not only increases access to capital to public companies it can also serve to provide more return on investment opportunities for private investors.

Licensing continues to be an integral part of the emerging biotech story. This is most evidenced by the degree to which the small company pipeline is partnered (43% of all emerging company clinical programs). This ranged from only 28% for Endocrine to 53% for Hematology programs. In all but two disease areas, (Metabolic and Psychiatry), the percent of the partnering increased with development stage of the drug candidate. This makes sense as the out-licensor has the potential to realize more value, and the in-licensor will, probabilistically, take on less risk with data from later stage trials. In eight of the fourteen disease areas analyzed, over half of Phase III programs were partnered, whereas for Phase II only three of the fourteen disease areas were more than 50% partnered (Respiratory, Gastrointestinal, and Ophthalmology). For Phase I, only Ophthalmology was over 50% partnered.

Some of the increase in total dollar amounts for acquisition of R&D-stage companies in the last few years can be attributed to just a few HCV-focused companies. After removing these outliers, we see fairly steady acquisition interest from large biopharma companies. The lack of a spike or large drop in a given year, or over consecutive years, suggests a strategic balance of collaboration versus acquisition at the R&D-stage, leading to programs being developed by a diverse group. However, consolidation does seem to be more the norm when emerging companies gain approval and approach profitability. The \$131.6 billion spent on market-stage acquisitions is more than all the investment (venture + IPO + FOPO) into US emerging therapeutic biotech combined (\$92.3 billion) over the last decade. Only five biotechs in the industry's history have escaped acquisition post-approval to, become large biopharma players themselves.

Since the first biotech company was formed in 1977, the industry has gone through several funding cycles. Many of the metrics analyzed in this report, with a few exceptions, point to the industry emerging from a recent

bust cycle to thriving once again. This reinvigorated sentiment is buttressed by sound policies such as the JOBS Act, FDASIA, 12 year data exclusivity for biologics, the R&D Tax Credit and the Orphan Drug Credit have helped reverse or buffer some of the challenges to maintaining a stable innovation ecosystem. It is imperative that a sound 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. Continued investment requires strong intellectual property protections, a regulatory system that is reflective of current and emerging medical science, and incentives for private and public sector investment in this innovative industry.

# Methodology

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

**Tagging and Categorizing:** 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 (peptide often) is being utilized and will have the modality tagged with vaccine instead of large. 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 (it is inflammation), but we chose to place it under GI.

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, it is labeled as Cardiovascular.

Osteoporosis falls under Endocrine, and Osteoarthritis was placed under "Other." Also under "Other" are Dermatology, Allergy, Musculoskeletal diseases, Osteoarthritis, Otology (ear diseases), Periodontitis, Urology/Genitourinary, non-viral liver diseases, fertility drugs, and treatments for side effects of chemotherapy or radiation.

### Data Sources and unique categorization for each category

**Venture Capital:** Four databases were combined to create the broadest study possible: BioCentury's BCIQ, Elsevier'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 2004 to 2013 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 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.

**Innovation score:** We grouped companies into two categories: 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 we include 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 includes 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, nutraceuticals, and medical foods.

**Round of Investment for Venture Capital:** 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 A round financings. If the A1, A2, A3 rounds occurred in 2011, 2012, and 2013, then these would be counted as one A round investment per year. This enables an accurate accounting of breadth of funding on a yearly basis.

**IPO:** BIO Industry Analysis tracks this 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.

**FOPO:** Biocentury was the primary data source. Only new shares issued in a follow-on offerings valued at above \$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 Stategic Transactions database and Recap (Thomson Reuters) were primary data sources. 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. We analyzed each Led company and partner for inclusion as an emerging company or large company, defined by below or above \$1 billion in sales, respectively.

**Acquisitions:** Primary data sources 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.

## References and Footnotes

- 1. Over the last 3 years, 60% of acquisitions contained Contingent Value Rights (CVRs) tied to future clinical, regulatory, and sales milestones. Some studies have shown that the percentage of milestones actually resulting in a payout is less than 40% (Life Sci VC Blog, http://lifescivc.com/2015/04/scorecard-of-biobuck-ma-earnouts). As discussed with licensing deal structures, future milestone payments are rarely realized in their entirety due to low probabilities of success experienced by the drug industry. Thus this report focuses on the upfront payments for both acquisitions and licensing deals.
- 2. The large biologics investment in 2014 exemplifies a trend of increased interest in biologics by venture capitalists: The percentage of biologics R&D (large molecule R&D, including vaccines) being funded continues to be at high levels, reaching 51% of total venture R&D funding in 2014 vs 27% in 2004.
- **3.** Adding private investments in public equity (PIPEs) to the analysis adds \$1.2 billion per year on average, and that annual amount has been fairly level since 2008.
- **4.** Hay, M., Thomas, D. Clinical development success rates for investigational drugs. Nature Biotechnology, 01/2014; 32(1):40-51. Based on this analysis, only 32% of drugs make it from Phase II to Phase III, and only 50% from Phase III to FDA Approval.
- 5. For US acquisitions, 2014 was the highest total spent for US emerging companies in a decade, at \$27 billion. US-based companies accounted for 81% on the total global acquisition amount, and 66% of the all acquisitions since 2005.
- 6. http://globalgenes.org/rare-diseases-facts-statistics/ (accessed April 2015)
- 7. https://www.bio.org/biovestudy

# **Appendix**

| vc                | 2005    | 2006    | 2007    | 2008    | 2009    | 2010    | 2011    | 2012    | 2013    | 2014    | 10 yr Total |
|-------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|-------------|
| Oncology          | \$689   | \$680   | \$1,353 | \$1,136 | \$919   | \$616   | \$923   | \$740   | \$1,042 | \$1,199 | \$9,296     |
| Infectious        | \$458   | \$522   | \$596   | \$435   | \$452   | \$323   | \$375   | \$171   | \$345   | \$528   | \$4,205     |
| Neurology         | \$473   | \$481   | \$493   | \$453   | \$532   | \$314   | \$184   | \$322   | \$375   | \$453   | \$4,079     |
| Platform          | \$227   | \$360   | \$208   | \$180   | \$221   | \$250   | \$141   | \$286   | \$369   | \$868   | \$3,109     |
| Other             | \$256   | \$283   | \$370   | \$266   | \$225   | \$320   | \$256   | \$367   | \$265   | \$321   | \$2,929     |
| Endocrine         | \$183   | \$430   | \$398   | \$209   | \$176   | \$77    | \$279   | \$284   | \$157   | \$272   | \$2,466     |
| Cardiovascular    | \$281   | \$299   | \$374   | \$221   | \$167   | \$141   | \$256   | \$283   | \$177   | \$56    | \$2,255     |
| Metabolic         | \$173   | \$288   | \$239   | \$93    | \$162   | \$176   | \$241   | \$371   | \$265   | \$161   | \$2,169     |
| Ophthalmology     | \$105   | \$174   | \$285   | \$138   | \$196   | \$92    | \$216   | \$107   | \$275   | \$293   | \$1,880     |
| Immunology        | \$67    | \$265   | \$77    | \$310   | \$157   | \$152   | \$57    | \$148   | \$171   | \$262   | \$1,666     |
| Hematology        | \$210   | \$126   | \$170   | \$109   | \$90    | \$104   | \$91    | \$150   | \$90    | \$47    | \$1,187     |
| Respiratory       | \$64    | \$157   | \$237   | \$169   | \$106   | \$154   | \$106   | \$65    | \$60    | \$49    | \$1,168     |
| Gastroinstestinal | \$146   | \$216   | \$128   | \$207   | \$39    | \$67    | \$66    | \$87    | \$52    | \$18    | \$1,026     |
| Psychiatry        | \$274   | \$129   | \$56    | \$36    | \$50    | \$39    | \$58    | \$111   | \$44    | \$154   |             |
| TOTAL             | \$3,606 | \$4,411 | \$4,984 | \$3,960 | \$3,491 | \$2,826 | \$3,249 | \$3,492 | \$3,686 | \$4,681 | \$38,385    |

Table A1. Venture capital, by major disease category - \$M invested per year. (Categories listed by largest 10 year total, top to bottom.)

| IPOs               | 2005  | 2006  | 2007  | 2008 | 2009    | 2010        | 2011  | 2012  | 2013    | 2014    | 10 yr Total |
|--------------------|-------|-------|-------|------|---------|-------------|-------|-------|---------|---------|-------------|
| Oncology           | \$266 | \$104 | \$50  | \$0  | \$0     | \$81        | \$248 | \$236 | \$958   | \$1,033 | \$2,976     |
| Hematology         | \$41  | \$106 | \$15  |      | \$950   | \$0         | \$0   |       | \$205   | \$309   | \$1,626     |
| Other              | \$0   | \$37  | \$0   |      | \$85    | \$30        | \$106 | \$81  | \$0     | \$1,212 | \$1,551     |
| Infectious Disease | \$52  | \$202 | \$172 |      | \$0     | \$123       | \$0   | \$140 | \$315   | \$420   | \$1,423     |
| Neurology          | \$108 | \$214 | \$152 | \$0  | \$68    | \$106       | \$82  | \$55  | \$0     | \$467   | \$1,252     |
| Endocrine          | \$0   | \$0   | \$155 | \$0  | \$0     | \$0         | \$0   | \$0   | \$0     | \$612   | \$767       |
| Metabolic          |       | \$0   | \$172 |      |         | \$0         | \$0   | \$50  | \$301   | \$176   | \$699       |
| Inflammation       | \$48  | \$60  | \$0   |      |         | \$17        | \$50  | \$120 | \$73    | \$302   | \$670       |
| Ophthamology       | \$0   | \$0   | \$0   |      |         | \$72        | \$0   | \$0   | \$234   | \$267   | \$573       |
| Gastrointestinal   |       | \$144 | \$86  | \$0  |         | \$188       | \$55  |       | \$25    | \$60    | \$557       |
| Cardiovascular     | \$17  | \$0   | \$0   | \$5  |         | \$90        | \$0   |       | \$134   | \$161   | \$407       |
| Respiratory        | \$121 | \$0   | \$69  | \$0  |         | \$0         | \$0   |       | \$72    | \$0     | \$262       |
| Platform           | \$0   | \$0   | \$0   |      |         | \$0         | \$0   | \$45  | \$70    | \$102   | \$217       |
| Psychiatry         |       | \$60  | \$0   | \$0  | \$0     | <b>\$</b> 0 | \$0   | \$0   | \$0     | \$33    | \$92        |
| TOTAL              | \$653 | \$926 | \$870 | \$5  | \$1,103 | \$706       | \$541 | \$727 | \$2,387 | \$5,154 | \$13,072    |

Table A2. IPO, by Disease - \$M invested per year. (Categories listed by largest 10 year total, top to bottom.)

| FOPO               | 2005    | 2006    | 2007    | 2008        | 2009    | 2010    | 2011    | 2012    | 2013    | 2014    | 10 yr Total |
|--------------------|---------|---------|---------|-------------|---------|---------|---------|---------|---------|---------|-------------|
| Oncology           | \$721   | \$474   | \$791   | \$174       | \$1,570 | \$644   | \$1,518 | \$1,782 | \$2,260 | \$2,090 | \$12,024    |
| Infectious Disease | \$750   | \$633   | \$0     | \$338       | \$1,765 | \$512   | \$572   | \$613   | \$1,049 | \$1,054 | \$7,285     |
| Neurology          | \$95    | \$157   | \$625   | \$242       | \$115   | \$463   | \$238   | \$531   | \$423   | \$1,712 | \$4,601     |
| Endocrine          | \$496   | \$1,018 | \$92    | \$51        | \$181   | \$140   | \$249   | \$657   | \$538   | \$255   | \$3,677     |
| Metabolic          | \$112   | \$664   | \$109   | \$81        | \$173   | \$0     | \$170   | \$662   | \$254   | \$949   | \$3,174     |
| Gastrointestinal   | \$119   | \$144   | \$149   | \$0         | \$190   | \$111   | \$294   | \$197   | \$342   | \$345   | \$1,890     |
| Cardiovascular     | \$492   | \$243   | \$35    |             | \$0     | \$76    | \$91    | \$114   | \$270   | \$345   | \$1,665     |
| Immunology         | \$105   | \$179   | \$84    | \$139       | \$244   | \$241   | \$58    | \$38    | \$175   | \$334   | \$1,596     |
| Other              | \$126   | \$37    | \$68    | \$0         | \$109   | \$0     | \$46    | \$70    | \$418   | \$646   | \$1,520     |
| Hematology         | \$212   | \$72    | \$16    |             | \$86    | \$270   | \$63    | \$18    | \$203   | \$403   | \$1,343     |
| Respiratory        | \$0     | \$0     | \$78    |             | \$100   | \$114   | \$96    | \$0     | \$337   | \$432   | \$1,157     |
| Ophthalmology      | \$83    | \$52    | \$0     |             | \$155   | \$62    | \$0     | \$146   | \$11    | \$284   | \$793       |
| Psychiatry         | \$0     | \$0     | \$12    |             | \$0     | \$0     | \$0     | \$22    |         | \$11    | \$45        |
| Platform           | \$32    | \$0     | \$0     | <b>\$</b> O | \$0     | \$0     |         | \$0     |         | \$0     | \$32        |
| TOTAL              | \$3,343 | \$3,673 | \$2,060 | \$1,023     | \$4,688 | \$2,633 | \$3,395 | \$4,850 | \$6,279 | \$8,857 | \$40,801    |

 Table A3. FOPO, by Disease - \$M invested per year. (Categories listed by largest 10 year total, top to bottom.)

| R&D-Stage<br>Licensing | 2005    | 2006    | 2007    | 2008    | 2009    | 2010    | 2011    | 2012    | 2013    | 2014    | 10 yr Total |
|------------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|-------------|
| Oncology               | \$579   | \$559   | \$726   | \$841   | \$919   | \$533   | \$1,139 | \$804   | \$874   | \$1,627 | \$8,602     |
| Neurology              | \$365   | \$253   | \$417   | \$624   | \$1,559 | \$251   | \$128   | \$231   | \$276   | \$586   | \$4,691     |
| Infectious Disease     | \$149   | \$570   | \$717   | \$218   | \$797   | \$304   | \$197   | \$257   | \$58    | \$196   | \$3,463     |
| Platform               | \$194   | \$87    | \$797   | \$270   | \$139   | \$230   | \$487   | \$71    | \$396   | \$142   | \$2,813     |
| Immunology             | \$664   | \$363   | \$50    | \$233   | \$296   | \$189   | \$259   | \$163   | \$261   | \$82    | \$2,560     |
| Endocrine              | \$10    | \$125   | \$354   | \$138   | \$113   | \$476   | \$588   | \$8     | \$96    | \$530   | \$2,437     |
| Cardiovascular         | \$213   | \$202   | \$180   | \$365   | \$175   | \$737   | \$72    | \$6     | \$120   | \$91    | \$2,161     |
| Other                  | \$31    | \$193   | \$222   | \$138   | \$107   | \$681   | \$98    | \$310   | \$95    | \$152   | \$2,027     |
| Metabolic              | \$65    | \$40    | \$105   | \$272   | \$185   | \$166   | \$33    | \$95    | \$62    | \$738   | \$1,760     |
| Gastrointestinal       | \$60    | \$54    | \$145   | \$148   | \$266   | \$0     | \$50    | \$20    | \$70    | \$758   | \$1,571     |
| Hematology             | \$28    | \$511   | \$75    | \$19    | \$102   | \$30    | \$25    | \$38    | \$66    | \$260   | \$1,154     |
| Psychiatry             | \$236   | \$20    | \$93    | \$22    | \$231   | \$32    | \$202   | \$11    | \$98    | \$25    | \$969       |
| Ophthalmology          | \$17    | \$110   | \$0     | \$53    | \$36    | \$25    | \$60    | \$163   | \$10    | \$418   | \$891       |
| Respiratory            | \$49    | \$151   | \$81    | \$41    | \$275   | \$52    | \$9     | \$1     | \$50    | \$57    |             |
| TOTAL                  | \$2,660 | \$3,238 | \$3,961 | \$3,381 | \$5,200 | \$3,706 | \$3,347 | \$2,177 | \$2,533 | \$5,662 | \$35,865    |

**Table A4.** R&D-Stage Licensing, by Disease - \$M invested per year. (Categories listed by largest 10 year total, top to bottom.)

| R&D-Stage<br>Acqusitions | 2005    | 2006    | 2007    | 2008    | 2009    | 2010    | 2011     | 2012    | 2013    | 2014    | 10 yr Total |
|--------------------------|---------|---------|---------|---------|---------|---------|----------|---------|---------|---------|-------------|
| Infectious Disease       | \$2,889 | \$1,461 | \$358   | \$916   | \$1,187 | \$0     | \$11,412 | \$2,131 | \$1,339 | \$5,827 | \$27,521    |
| Oncology                 | \$614   | \$1,098 | \$5,014 | \$726   | \$1,773 | \$2,833 | \$2,218  | \$2,175 | \$2,616 | \$1,435 | \$20,503    |
| Platform                 | \$673   | \$1,297 | \$427   | \$946   | \$29    | \$598   | \$10     | \$111   | \$51    | \$175   | \$4,317     |
| Immunology               | \$0     | \$68    | \$933   | \$1,012 | \$221   | \$102   | \$186    | \$1,272 | \$0     | \$260   | \$4,054     |
| Cardiovascular           | \$33    | \$2,244 | \$350   | \$538   | \$153   | \$165   | \$10     | \$3     | \$336   | \$42    | \$3,873     |
| Neurology                | \$117   | \$581   | \$327   | \$81    | \$703   | \$695   | \$210    | \$46    | \$37    | \$952   | \$3,748     |
| Other                    | \$68    | \$0     | \$545   | \$1,553 | \$302   | \$70    | \$175    | \$9     | \$0     | \$0     | \$2,723     |
| Endocrine                | \$0     | \$17    | \$620   |         | \$0     | \$472   | \$71     | \$315   | \$730   | \$107   | \$2,333     |
| Gastrointestinal         | \$44    | \$332   | \$0     |         |         | \$390   | \$21     | \$0     | \$0     | \$1,027 | \$1,813     |
| Ophthalmology            | \$0     | \$1,128 | \$0     |         | \$298   | \$0     |          |         | \$160   | \$67    | \$1,652     |
| Respiratory              | \$186   | \$0     | \$0     |         | \$0     | \$204   | \$328    | \$178   | \$600   | \$0     | \$1,496     |
| Metabolic                | \$0     | \$18    | \$0     | \$30    |         | \$22    | \$610    | \$293   | \$74    | \$89    | \$1,136     |
| Hematology               | \$0     |         | \$0     | \$400   | \$255   | \$0     | \$0      | \$94    | \$240   | \$0     | \$989       |
| Psychiatry               | \$0     |         | \$29    | \$0     | \$0     | \$226   |          | \$0     | \$0     | \$0     |             |
| TOTAL                    | \$4,625 | \$8,244 | \$8,603 | \$6,203 | \$4,923 | \$5,777 | \$15,250 | \$6,627 | \$6,182 | \$9,979 | \$76,413    |

**Table A5.** R&D-Stage Acquisitions, by Disease - \$M invested per year. (Categories listed by largest 10 year total, top to bottom.)

| Disease-Subindication             | 2005  | 2006  | 2007    | 2008    | 2009  | 2010  | 2011  | 2012  | 2013    | 2014    |
|-----------------------------------|-------|-------|---------|---------|-------|-------|-------|-------|---------|---------|
| Oncology - Oncology               | \$689 | \$680 | \$1,353 | \$1,136 | \$919 | \$616 | \$923 | \$740 | \$1,042 | \$1,199 |
| CV - Hypercholesterolemia         | \$23  | \$6   | \$29    | \$12    | \$2   | \$13  | \$51  | \$16  | \$54    | \$0     |
| CV - Hypertension                 | \$49  | \$0   | \$3     | \$10    | \$11  | \$25  | \$3   | \$10  | \$13    | \$1     |
| CV - Other Indication             | \$178 | \$288 | \$332   | \$191   | \$115 | \$93  | \$202 | \$257 | \$109   | \$55    |
| CV - Multiple Indications         | \$30  | \$5   | \$10    | \$8     | \$39  | \$10  | \$0   | \$0   | \$0     | \$0     |
| ID - Antimicrobial g+             | \$65  | \$106 | \$169   | \$31    | \$134 | \$50  | \$74  | \$70  | \$65    | \$101   |
| ID - Antimicrobial g-             | \$3   | \$13  | \$21    | \$47    | \$2   | \$5   | \$45  | \$12  | \$70    | \$10    |
| ID - Antimicrobial broad          | \$169 | \$142 | \$87    | \$73    | \$19  | \$114 | \$65  | \$0   | \$28    | \$147   |
| ID - Anti-fungal                  | \$58  | \$16  | \$6     | \$39    | \$75  | \$6   | \$22  | \$3   | \$41    | \$102   |
| ID - Antiviral - other            | \$10  | \$44  | \$97    | \$25    | \$95  | \$20  | \$61  | \$14  | \$50    | \$92    |
| ID - HCV                          | \$91  | \$82  | \$85    | \$89    | \$43  | \$25  | \$12  | \$0   | \$21    | \$13    |
| ID - HIV                          | \$44  | \$56  | \$84    | \$50    | \$16  | \$18  | \$42  | \$15  | \$11    | \$0     |
| ID - Vaccine                      | \$19  | \$62  | \$19    | \$82    | \$63  | \$84  | \$53  | \$56  | \$59    | \$36    |
| ID - Other Indication             | \$0   | \$0   | \$29    | \$0     | \$6   | \$1   | \$0   | \$0   | \$0     | \$27    |
| ID - Multiple Indications         | \$0   | \$0   | \$0     | \$0     | \$0   | \$0   | \$0   | \$0   | \$0     | \$0     |
| Immunology - Arthritis            | \$26  | \$58  | \$56    | \$86    | \$5   | \$29  | \$8   | \$56  | \$0     | \$109   |
| Immunology - Psoriasis            | \$0   | \$0   | \$0     | \$6     | \$2   | \$2   | \$0   | \$11  | \$10    | \$74    |
| Immunology - Other Indication     | \$28  | \$115 | \$7     | \$122   | \$106 | \$83  | \$49  | \$70  | \$116   | \$79    |
| Immunology - Multiple Indications | \$13  | \$92  | \$15    | \$97    | \$44  | \$38  | \$0   | \$11  | \$45    | \$0     |
| Endocrine - T2D                   | \$103 | \$179 | \$165   | \$138   | \$23  | \$37  | \$180 | \$219 | \$29    | \$229   |
| Endocrine - T1D                   | \$20  | \$51  | \$34    | \$5     | \$16  | \$8   | \$3   | \$0   | \$14    | \$3     |
| Endocrine - Other Indication      | \$60  | \$201 | \$200   | \$66    | \$138 | \$32  | \$96  | \$65  | \$114   | \$40    |
| Endocrine - Multiple Indications  | \$0   | \$0   | \$0     | \$0     | \$0   | \$0   | \$0   | \$0   | \$0     | \$0     |
| Metabolic - Obesity               | \$58  | \$55  | \$7     | \$37    | \$11  | \$32  | \$73  | \$21  | \$35    | \$12    |
| Metabolic - Genetic Disorder      | \$65  | \$63  | \$92    | \$29    | \$100 | \$31  | \$133 | \$235 | \$97    | \$135   |
| Metabolic - Other Indication      | \$19  | \$47  | \$96    | \$19    | \$51  | \$113 | \$35  | \$115 | \$133   | \$14    |
| Metabolic - Multiple Indications  | \$31  | \$122 | \$44    | \$8     | \$0   | \$0   | \$0   | \$0   | \$0     | \$0     |
| Psychiatry - Schizophrenia        | \$86  | \$56  | \$14    | \$0     | \$2   | \$0   | \$0   | \$19  | \$18    | \$17    |
| Psychiatry - Depression           | \$80  | \$23  | \$2     | \$36    | \$4   | \$38  | \$27  | \$75  | \$7     | \$121   |
| Psychiatry - Other Indication     | \$109 | \$50  | \$40    | \$0     | \$44  | \$0   | \$31  | \$17  | \$19    | \$16    |
| Psychiatry - Multiple Indications | \$0   | \$0   | \$0     | \$0     | \$0   | \$0   | \$0   | \$0   | \$0     | \$0     |

**Table A6**. Venture capital, by indication - \$M invested per year. (continued on next page)

| Disease-Subindication              | 2005    | 2006    | 2007    | 2008    | 2009    | 2010    | 2011    | 2012    | 2013    | 2014    |
|------------------------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Neurology - Pain                   | \$150   | \$283   | \$266   | \$158   | \$245   | \$124   | \$106   | \$161   | \$97    | \$137   |
| Neurology - Parkinson's            | \$8     | \$8     | \$28    | \$0     | \$0     | \$26    | \$10    | \$15    | \$39    | \$117   |
| Neurology - Alzheimer's            | \$83    | \$17    | \$15    | \$44    | \$47    | \$48    | \$31    | \$34    | \$54    | \$25    |
| Neurology - MS                     | \$65    | \$20    | \$48    | \$129   | \$40    | \$2     | \$9     | \$17    | \$21    | \$5     |
| Neurology - Other Indication       | \$159   | \$102   | \$134   | \$31    | \$181   | \$66    | \$21    | \$78    | \$134   | \$169   |
| Neurology - Multiple Indications   | \$8     | \$51    | \$2     | \$91    | \$19    | \$50    | \$8     | \$18    | \$30    | \$0     |
| Respiratory - Asthma               | \$35    | \$56    | \$137   | \$39    | \$52    | \$31    | \$9     | \$3     | \$6     | \$36    |
| Respiratory - COPD                 | \$0     | \$6     | \$37    | \$20    | \$0     | \$59    | \$49    | \$53    | \$42    | \$0     |
| Respiratory - Other Indication     | \$29    | \$95    | \$56    | \$106   | \$22    | \$65    | \$34    | \$6     | \$13    | \$13    |
| Respiratory - Multiple Indications | \$0     | \$0     | \$8     | \$4     | \$32    | \$0     | \$14    | \$3     | \$0     | \$0     |
| Hematology - Blood Stimulator      | \$148   | \$26    | \$129   | \$3     | \$3     | \$22    | \$52    | \$63    | \$3     | \$0     |
| Hematology - Coagulation           | \$0     | \$69    | \$0     | \$40    | \$25    | \$22    | \$0     | \$7     | \$11    | \$37    |
| Hematology - Other Indication      | \$61    | \$29    | \$34    | \$65    | \$56    | \$60    | \$39    | \$80    | \$77    | \$10    |
| Hematology - Multiple Indications  | \$1     | \$2     | \$6     | \$0     | \$6     | \$0     | \$0     | \$0     | \$0     | \$0     |
| GI - IBS                           | \$45    | \$84    | \$97    | \$85    | \$39    | \$18    | \$30    | \$30    | \$26    | \$11    |
| GI - GERD                          | \$0     | \$30    | \$0     | \$5     | \$0     | \$0     | \$0     | \$0     | \$0     | \$0     |
| GI - Crohn's                       | \$15    | \$66    | \$3     | \$105   | \$0     | \$0     | \$0     | \$16    | \$0     | \$0     |
| GI - Ulcerative Colitis            | \$0     | \$6     | \$2     | \$6     | \$0     | \$0     | \$0     | \$19    | \$1     | \$2     |
| GI - Other Indication              | \$87    | \$30    | \$26    | \$6     | \$0     | \$49    | \$35    | \$22    | \$26    | \$5     |
| GI - Multiple Indications          | \$0     | \$0     | \$0     | \$0     | \$0     | \$0     | \$1     | \$0     | \$0     | \$0     |
| Ophthalmology                      | \$105   | \$174   | \$285   | \$138   | \$196   | \$92    | \$216   | \$107   | \$275   | \$293   |
| PLATFORM                           | \$227   | \$360   | \$208   | \$180   | \$221   | \$250   | \$141   | \$286   | \$369   | \$868   |
| Other - Allergy                    | \$25    | \$6     | \$0     | \$0     | \$0     | \$0     | \$0     | \$0     | \$12    | \$41    |
| Other - Dermatology                | \$13    | \$90    | \$60    | \$49    | \$62    | \$81    | \$80    | \$72    | \$110   | \$110   |
| Other - Renal                      | \$52    | \$98    | \$68    | \$67    | \$53    | \$71    | \$27    | \$103   | \$45    | \$70    |
| Other - Chemo/Rad side effects     | \$30    | \$0     | \$33    | \$0     | \$10    | \$20    | \$44    | \$58    | \$0     | \$0     |
| Other - Other Indication           | \$57    | \$53    | \$109   | \$52    | \$47    | \$84    | \$35    | \$134   | \$51    | \$100   |
| Other - Multiple Indications       | \$79    | \$36    | \$100   | \$97    | \$53    | \$64    | \$69    | \$0     | \$46    | \$0     |
| Total                              | \$2,917 | \$3,731 | \$3,631 | \$2,824 | \$2,572 | \$2,210 | \$2,326 | \$2,752 | \$2,644 | \$3,482 |

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