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Poor R&D Productivity as a Self-Inflicted Injury: Who's Missing the Most Toes, and Why

- Please see the SSR Health YouTube channel for podcasts of recent research
- R&D productivity can be measured, and thus managed, far better than is reflected in current practice
- Using metrics produced with a combination of US patent data and company disclosures, we calculate / identify:
  - *economic returns to R&D spending (the relationship btw Yr1 R&D and Yr10 adjusted earnings)*
  - *the number of quality-adjusted ideas produced per $M of R&D spend*
  - *the average quality of ideas produced*
  - *the pre-phase 3 research areas that account for at least 80 percent of each company's innovation; and*
  - *each company's rank v. peers in these key research areas*
- The related analyses identify 5 addressable causes of poor R&D productivity:
  1. *Companies tend to move their own discoveries into development, without fully considering whether externally available compounds would be a better use of development dollars.* ***LLY****,* ***AMGN****, and* ***AZN*** *are worst in class on this metric;* ***BMY****,* ***PFE****, and* ***Roche*** *are best-in-class*
  2. *A large percentage of companies' research activity takes place in research areas where the company is too low ranking for its efforts to be worthwhile. Across the research areas that account for 80 percent of pre-phase 3 innovation, the typical company has an average rank of 8th.* ***LLY*** *is worst-in-class among the large caps on this metric with an average rank of 12th;* ***BMY*** *and* ***Roche*** *are best-in-class with average ranks of 2nd*
  3. *Lack of cost discipline:* ***JNJ****,* ***GSK****,* ***NVS****,* ***LLY*** *and* ***SNY*** *all consistently spend much more than peers to produce a given quality-adjusted amount of innovation;* ***BMY*** *consistently spends less than peers*
  4. *Poor average quality of innovation:* ***Bayer****,* ***GSK, LLY****,* ***MRK****, and* ***SNY*** *consistently produce innovation that is of less than average quality ('per unit' of innovation) than peers;* ***BMY****,* ***CELG*** *and* ***VRTX*** *all consistently produce innovation of above average quality*
  5. *Negative scale economies both across (larger firms are less R&D productive than smaller firms) and within (as firms grow, they become less R&D productive) firms. Only* ***VRTX*** *has been able to substantially grow its real R&D spending without meaningful declines in R&D productivity*
- These and other R&D productivity metrics covering the 22 largest publicly-traded companies (by R&D spending) are available in a comprehensive benchmarking report at hiddenpipeline.com

Premise

R&D productivity can be measured well enough to: 1) establish which companies are more or less productive than their peers; and 2) give some indication of changes that underperforming companies can make to substantially improve their performance

Managements and investors have long been aware that R&D productivity is weak; left largely un-addressed, all indications are that the average company's economic returns to R&D spending now are below costs of capital. Yet there is still no consensus on how R&D productivity should be measured. Lacking credible metrics, managements fail to set operational goals and hold their employees accountable for meeting these; and, investors have no objective productivity criteria for holding managements responsible

Subjective estimates of R&D productivity tend to fill the void; as incomplete metrics, these tend to raise false hopes, and in so doing ease the pressure on managements just when efforts to improve productivity should be mounted far more aggressively. A rising number of NME/NBE[1]'s filed or approved is a favorite. Increased filings and approvals are plainly a good thing, but without an understanding of what was spent to generate these outcomes, how these investments compare to the earnings potential of the corresponding new products, and whether a given level of increase reflects anything other than the sporadic nature of research output, the filings/approvals number can be grossly misleading

Perhaps worst of all, sizable contingencies argue that R&D productivity simply cannot be measured – it's too complex, the timeframes are too long, and so forth. This emphatically is not true, and often rings of simple self-preservation

We make no assertion that our metrics are millimeter precise, or that we've captured all of R&D productivity's moving parts. What we have done is develop a workable empiric foundation for determining which companies are more or less productive, and for providing actionable levels of insight as to what underperforming companies can do to improve. There is no reason for managements not to act, or for investors not to hold managements more immediately accountable for raising their organizations' R&D productivity

Internal bias

Despite the fact that the large R&D based companies each generate a very small share of global innovation (1.3% on average), most dedicate very large percentages (70% on average) of their development spending to their own discoveries (**Exhibit 1**). In effect, the companies can be described as generally ignoring externally-generated discoveries in order to focus development spending on internally-generated discoveries. If the internally-generated discoveries were of higher average quality than those available externally this might make sense, but that's not the case (see next). We calculate a simple 'internal bias index' by dividing the percentage of development spending dedicated to the company's own discoveries by the same company's share of global biomedical innovation. Companies with relatively low shares of global innovation but whose development pipelines consist largely of their own discoveries have high (unfavorable) scores, and vice versa. Among the large cap names, **LLY, AMGN, and AZN** have the highest internal bias scores; **BMY, PFE,** and **Roche** have the lowest internal bias scores (**Exhibit 1**, again). We believe that high rates of

[1] New Molecular Entity / New Biologic Entity

internal bias – even for the companies with the most favorable scores – are a major *addressable* contributor to poor R&D productivity

Exh 1: Internal bias index

Company	(a) Company's own discoveries as share of clinical development projects	(b) Company innovation as share of all source biomed innovation	(a) : (b) Ratio (Internal bias index, LOWER IS BETTER)
Bristol-Myers Squibb	73.0%	3.2%	22.5
Pfizer	74.2%	3.1%	23.9
Roche	79.0%	3.3%	24.1
Sanofi	64.8%	2.3%	28.5
Johnson & Johnson	68.9%	2.0%	33.9
Merck	63.8%	1.8%	35.1
GlaxoSmithKline	62.4%	1.7%	36.5
Novartis	70.2%	1.9%	36.8
AstraZeneca	59.0%	1.4%	43.1
Vertex	76.5%	1.5%	52.6
AbbVie	52.5%	1.0%	54.4
Amgen	82.3%	1.4%	58.1
Bayer	71.4%	0.9%	81.7
Allergan	60.0%	0.6%	95.8
Celgene	50.0%	0.5%	97.9
Eli Lilly	78.7%	0.6%	131.1
Biogen Idec	54.2%	0.4%	154.6
Gilead	73.5%	0.4%	185.0
Shire	38.9%	0.1%	338.0
Novo Nordisk	89.2%	0.2%	439.2
Regeneron	90.0%	0.1%	638.0
Alexion	100.0%	0.0%	8,012.4
Peer group wtd avg	**69.7%**	**1.3%**	**54.0**

Sources: Bloomberg; AcclaimIP; SSR Hidden Pipeline Analysis

Lack of focus

Not even the largest R&D spender can fund active world class discovery efforts in all possible research areas. As such, companies focus their efforts in a select group of research areas; however most fail to achieve world class ranks (e.g. 1st, 2nd, or 3rd) in the subset of research areas they've targeted

For each of the 22 largest US-listed companies (by R&D spending) we identified the research areas accounting for at least 80 percent of each company's pre-phase III (i.e. from discovery to phase II) innovation. We then calculated each company's rank in each of its key research areas, and use this as an index of whether companies are or are not actively managing their early- to mid-stage research such that they achieve high average rankings across the research areas they've targeted

The companies' average rank in their key research areas is 8th (**Exhibit 2**). I.e., *most companies are actively conducting research in areas where they have little or no hope of producing a commercially viable result*, an unforced error

that many companies compound by prioritizing these non-competitive discoveries in their development programs (**Exhibit 1**, again)

Exh 2: Relative performance in top therapeutic areas

Company	Number of top therapeutic areas*	Average rank in top therapeutic areas	Share of top therapeutic areas with top 3 rank
Bristol-Myers Squibb	11	1.9	73%
Roche	15	2.0	80%
Pfizer	22	2.5	77%
Vertex	7	4.2	43%
Sanofi	26	4.2	54%
Johnson & Johnson	27	4.8	52%
Amgen	11	5.3	45%
Novartis	28	5.3	52%
Merck	24	5.4	46%
GlaxoSmithKline	18	6.0	39%
Gilead	7	6.4	43%
AstraZeneca	24	7.1	33%
Allergan	23	8.1	30%
Celgene	8	8.4	25%
AbbVie	22	9.4	23%
Bayer	23	10.3	13%
Novo Nordisk	12	10.8	25%
Eli Lilly	16	11.7	13%
Biogen Idec	8	13.1	13%
Regeneron	5	13.7	20%
Shire	12	15.4	0%
Alexion	3	21.4	0%
Peer group wtd avg	**16.0**	**8.1**	**36.3%**

*ATC codes representing 80% of the Hidden Pipeline
Sources: Bloomberg; AcclaimIP; SSR Hidden Pipeline Analysis

The best in class company is **BMY**, who has an average rank of 1.9 (**Exhibit 3**, column 'f') in the 11 research areas that account for 82 pct (column 'c') of its pre-phase 3 innovation. **BMY** is closely followed by **Roche** and **PFE**, who have average ranks in their targeted research areas of 2.0 and 2.5, respectively. **ALXN** is worst in class among the 22-largest R&D spenders with an average rank of 21.4; among the large caps **LLY** is worst in class with an average rank of 11.7 (**Exhibit 4**, column 'f') across the 16 research areas that account for 80 pct (column 'c') of the company's pre-phase 3 innovation. **LLY** ranks first in none of its targeted research areas (column 'g') and among the top 3 in only 2 research areas (columns 'h' and 'i')

Exh 3: BMY rank v. peers in the research areas that account for at least 80 percent of the company's pre-phase 3 innovation

									Sales wtd.	
(a)	(b)	(c)	(d)	(e)	(f)	(g)	(h)	(i)	(j)	(k)
ATC	Description	Share of BMY Hidden Pipeline	Share of peer group Hidden Pipeline	ATC share of BMY innovation by grant year (3 yr MA)	BMY rank v. peers	#1 ranked peer	#2 ranked peer	#3 ranked peer	*Share of BMY Hidden Pipeline*	*Share of peer group Hidden Pipeline*
L03AB	Interferons	21.4%	11.4%		1	BMY	PFE	MRK	13.8%	7.8%
L01XC	Monoclonal Antibodies	13.4%	13.0%		3	ROCHE	PFE	BMY	22.3%	22.9%
L04AB	Tumor Necrosis Factor Alpha (Tnf-A) Inhibitors	9.5%	4.9%		1	BMY	AMGN	GSK	20.4%	11.1%
L01XX	Other Antineoplastic Agents	8.8%	8.8%		2	VRTX	BMY	ROCHE	7.1%	7.6%
M09AB	Enzymes	8.1%	10.4%		4	ROCHE	SNY	PFE	0.3%	0.4%
L04AC	Interleukin Inhibitors	5.8%	2.9%		1	BMY	ROCHE	PFE	2.8%	1.5%
B01	Antithrombotic Agents	5.1%	3.2%		1	BMY	ROCHE	JNJ	11.2%	7.3%
A10B	Blood Glucose Lowering Drugs, Excluding Insulins	3.5%	2.8%		1	BMY	AZN	ROCHE	0.6%	0.5%
L04XX	Other Immunosuppressants	2.2%	2.9%		4	PFE	CELG	ROCHE	1.1%	1.5%
L01XE	Protein Kinase Inhibitors	1.9%	2.8%		5	PFE	VRTX	SNY	1.9%	3.0%
J05XX	Other Antivirals For Systemic Use	1.8%	0.7%		1	BMY	ROCHE	MRK	1.0%	0.4%
	Subtotals / avgs	**82%**	**63.8%**		**1.9**	**6**	**1**	**1**	**82.6%**	**64.0%**
	Cumulative share of ATCs with at least given ranking					*54.5%*	*63.6%*	*72.7%*		

Source: SSR Hidden Pipeline Analysis

Exh 4: LLY rank v. peers in the research areas that account for at least 80 percent of the company's pre-phase 3 innovation

									Sales wtd.	
(a)	(b)	(c)	(d)	(e)	(f)	(g)	(h)	(i)	(j)	(k)
ATC	Description	Share of LLY Hidden Pipeline	Share of peer group Hidden Pipeline	ATC share of LLY innovation by grant year (3 yr MA)	LLY rank v. peers	#1 ranked peer	#2 ranked peer	#3 ranked peer	*Share of LLY Hidden Pipeline*	*Share of peer group Hidden Pipeline*
A10B	Blood Glucose Lowering Drugs, Excluding Insulins	10.5%	2.8%		7	BMY	AZN	ROCHE	2.0%	0.5%
M09AB	Enzymes	9.7%	10.4%		15	ROCHE	SNY	PFE	0.3%	0.4%
L01XC	Monoclonal Antibodies	9.2%	13.0%		15	ROCHE	PFE	BMY	15.9%	22.9%
L04AB	Tumor Necrosis Factor Alpha (Tnf-A) Inhibitors	8.3%	4.9%		12	BMY	AMGN	GSK	18.5%	11.1%
L03AB	Interferons	7.4%	11.4%		15	BMY	PFE	MRK	4.9%	7.8%
L01XX	Other Antineoplastic Agents	7.2%	8.8%		16	VRTX	BMY	ROCHE	6.1%	7.6%
B01	Antithrombotic Agents	6.0%	3.2%		11	BMY	ROCHE	JNJ	13.6%	7.3%
L01XE	Protein Kinase Inhibitors	5.7%	2.8%		9	PFE	VRTX	SNY	6.0%	3.0%
L04XX	Other Immunosuppressants	3.1%	2.9%		15	PFE	CELG	ROCHE	1.6%	1.5%
G03XX	Other Sex Hormones And Modulators	2.6%	0.4%		2	PFE	LLY	BMY	1.3%	0.2%
G04BE	Drugs Used In Erectile Dysfunction	2.5%	0.6%		6	MRK	PFE	JNJ	1.2%	0.3%
J02	Antimycotics For Systemic Use	1.9%	0.3%		3	SNY	MRK	LLY	0.8%	0.1%
N05A	Antipsychotics	1.8%	0.5%		6	BMY	SNY	MRK	3.8%	1.0%
J01	Antibacterials For Systemic Use	1.5%	1.6%		15	PFE	ABBV	NVS	5.3%	6.0%
N02C	Antimigraine Preparations	1.4%	1.0%		13	MRK	BAYER	AZN	0.4%	0.3%
N06A	Antidepressants	1.2%	0.6%		8	AZN	BMY	PFE	2.1%	1.0%
	Subtotals / avgs	**80.1%**	**65.1%**		**11.7**	**0**	**1**	**1**	**83.8%**	**70.9%**
	Cumulative share of ATCs with at least given ranking					*0.0%*	*6.3%*	*12.5%*		

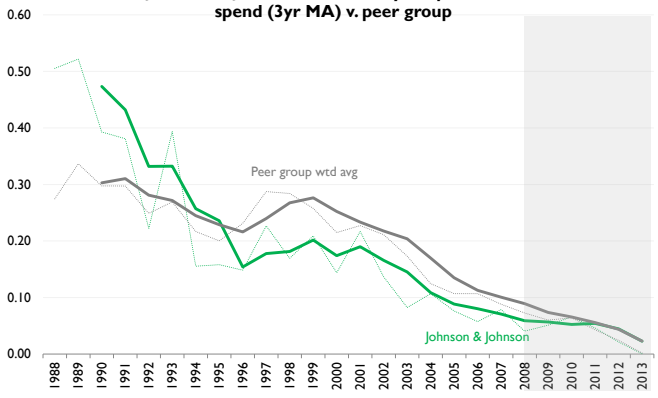
Source: SSR Hidden Pipeline Analysis

Simple 'dollars per idea' inefficiency

The number of quality-adjusted ideas produced per dollar of R&D spending varies widely across companies; some companies simply spend too much to generate a given amount of innovation as compared to their peers

Among the larger cap names, **JNJ, GSK, NVS, LLY** and **SNY** all consistently produce fewer quality-adjusted 'units' of innovation per R&D dollar spent than peers (**Exhibits 5a** thru **5e**); **AZN** was dramatically below the peer average for most of its history, and has only recently reached the (falling) peer average (**Exhibit 5f**). **BMY** (**Exhibit 6**) is best in class among the larger cap names

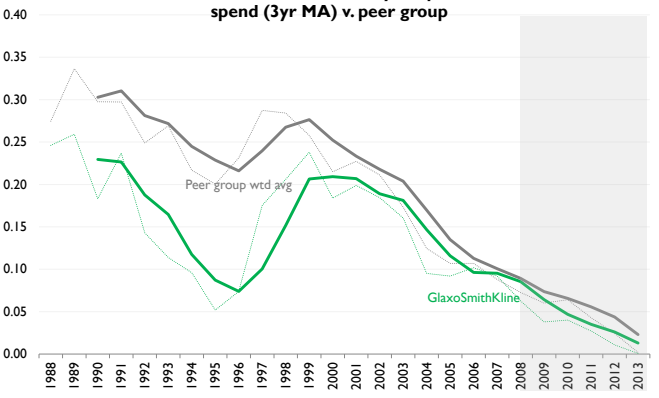
Exh 5a: Johnson & Johnson innovation yield per $1M real R&D spend (3yr MA) v. peer group



*'Innovation' quantified using a formula that captures raw patent grants; citation accumulation, and vintage
Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution

Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

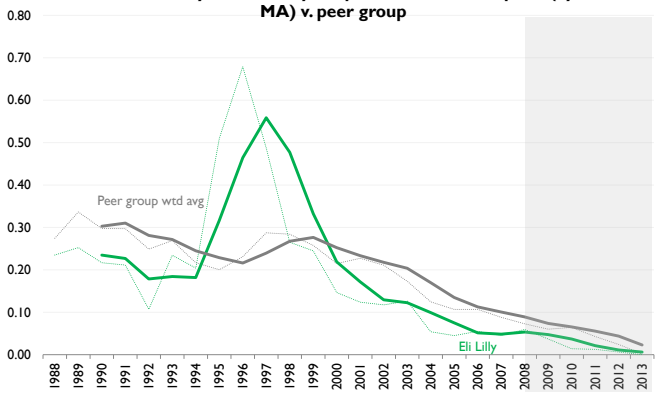
Exh 5b: GlaxoSmithKline innovation yield per $1M real R&D spend (3yr MA) v. peer group



*'Innovation' quantified using a formula that captures raw patent grants; citation accumulation, and vintage
Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution

Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

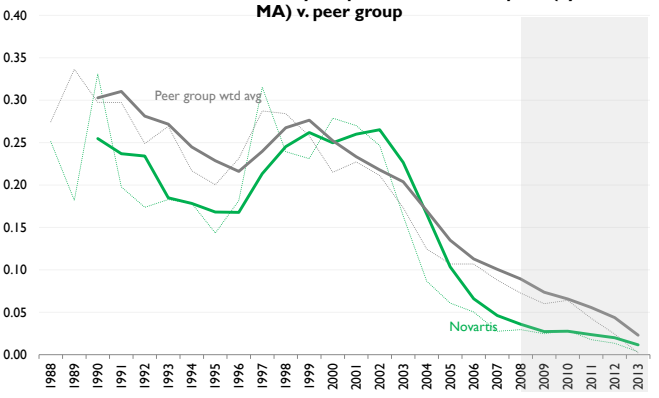
Exh 5c: Eli Lilly innovation yield per $1M real R&D spend (3yr MA) v. peer group



*'Innovation' quantified using a formula that captures raw patent grants; citation accumulation, and vintage
Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution

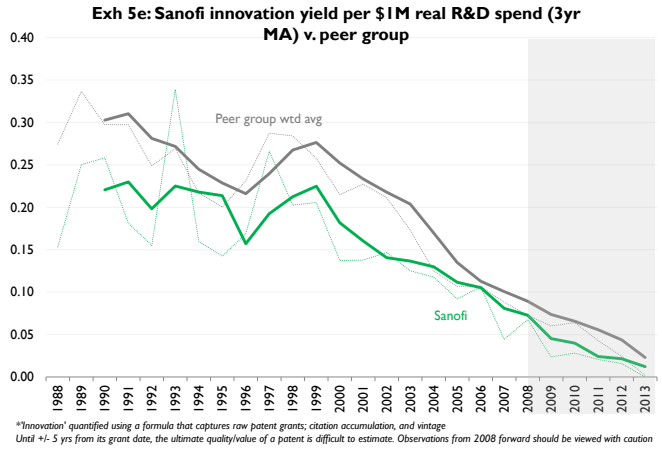
Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

Exh 5d: Novartis innovation yield per $1M real R&D spend (3yr MA) v. peer group

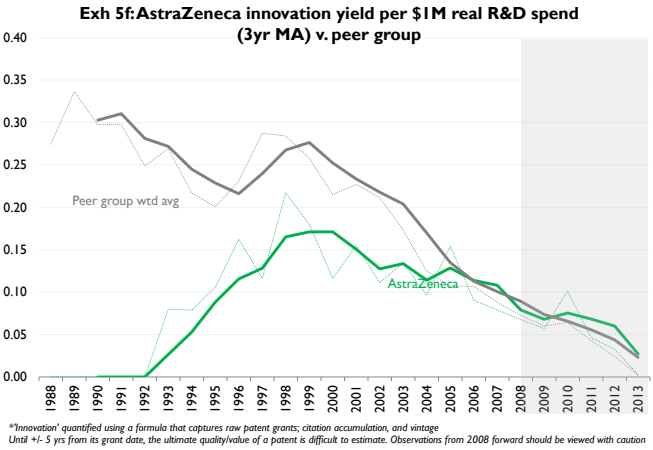


*'Innovation' quantified using a formula that captures raw patent grants; citation accumulation, and vintage
Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution

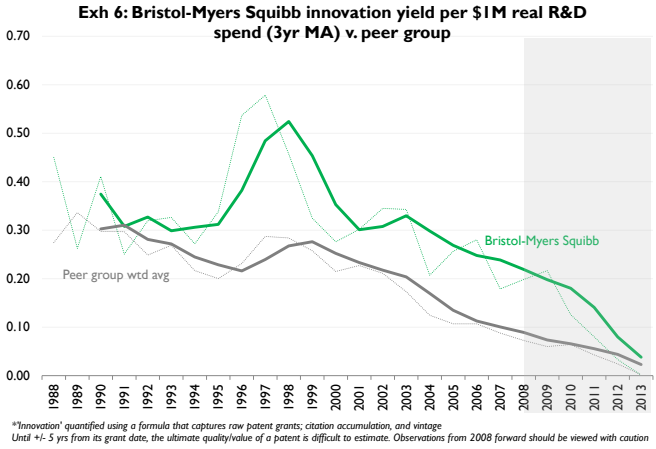
Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions



Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions



Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions



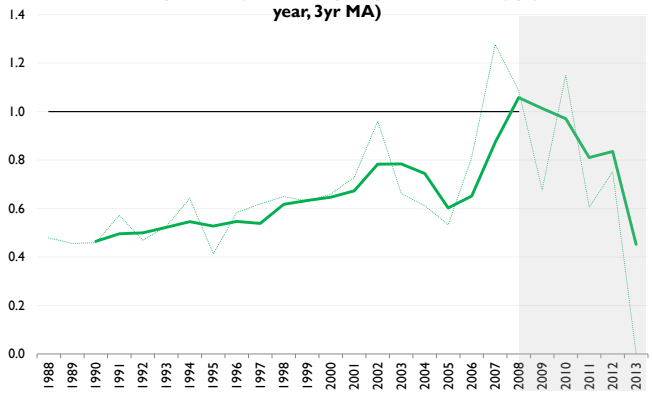
Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

Low average quality

As is the case with R&D spending per idea, the average apparent quality[2] of ideas generated varies widely across companies, and some companies have consistently produced innovation of lower average quality than peers'. **Bayer, GSK, LLY, MRK**, and **SNY** (**Exhibits 7a** thru **7e**) all have average qualities of innovation that are consistently below the peer average. Conversely **BMY, CELG**, and **VRTX** all have average quality levels that consistently exceed the peer average (**Exhibit 8a** thru **8c**)

[2] We estimate average quality using patents, and patent citations. Because patents must reference (i.e. 'cite') earlier-filed patents whose claims inform or limit the claims of the later filed patents, citations received by a patent from other later-filed patents are an indicator of: 1) the extent to which the earlier-filed patent lies within an area of discovery that is of interest to other inventors; and 2) the extent to which the earlier-filed patent's claims are relevant to claims made by later inventors. Other than being early and conducting meaningful research in important areas, companies have few if any means of influencing the number of citations a given patent will receive. We recognize that companies who file more patents for a given invention would tend to have lower apparent quality readings simply because the citations gained by the invention would be spread across more patents. Within the scope of patents we're analyzing for this metric – those associated with phase II and earlier projects – the evidence indicates that companies' patenting behaviors are very consistent, which we believe limits this potential source of bias

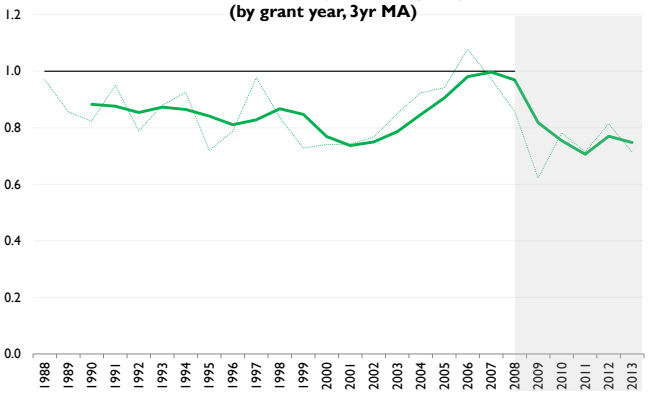
Exh 7a: Bayer average relative quality of innovation (by grant year, 3yr MA)



**Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution*

Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

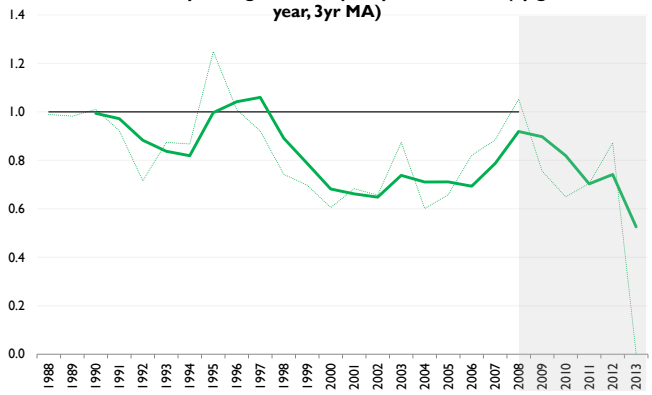
Exh 7b: GlaxoSmithKline average relative quality of innovation (by grant year, 3yr MA)



**Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution*

Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

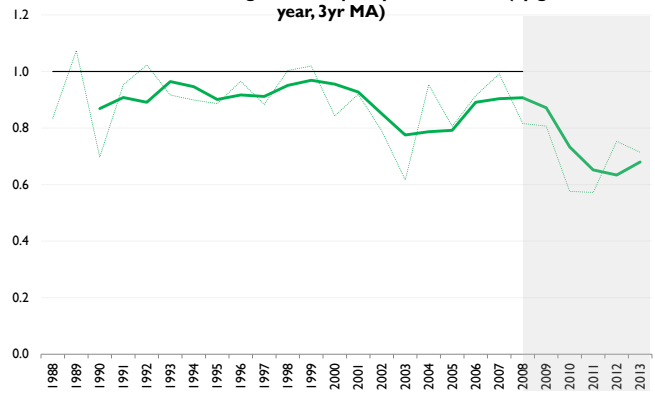
Exh 7c: Eli Lilly average relative quality of innovation (by grant year, 3yr MA)



**Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution*

Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

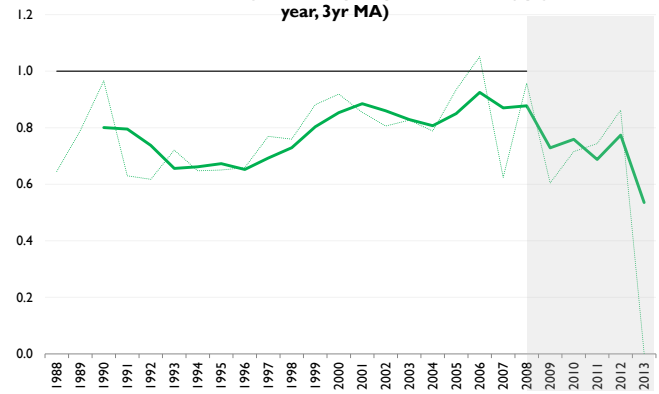
Exh 7d: Merck average relative quality of innovation (by grant year, 3yr MA)



**Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution*

Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

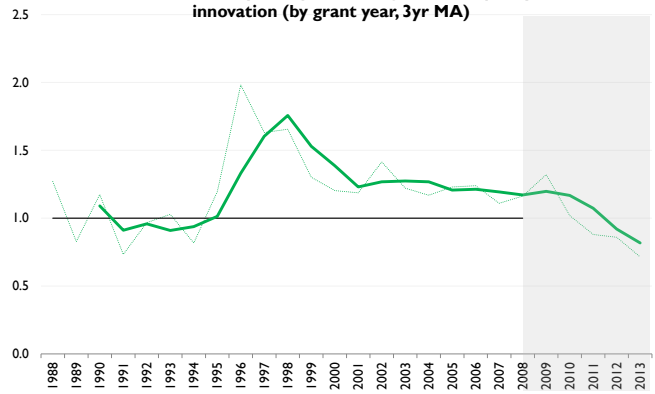
Exh 7e: Sanofi average relative quality of innovation (by grant year, 3yr MA)



**Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution*

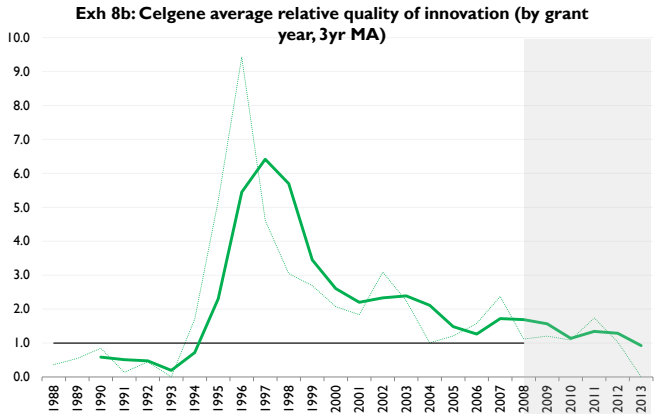
Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

Exh 8a: Bristol-Myers Squibb average relative quality of innovation (by grant year, 3yr MA)



**Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution*

Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions



*Until +/- 5 yrs from its grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution

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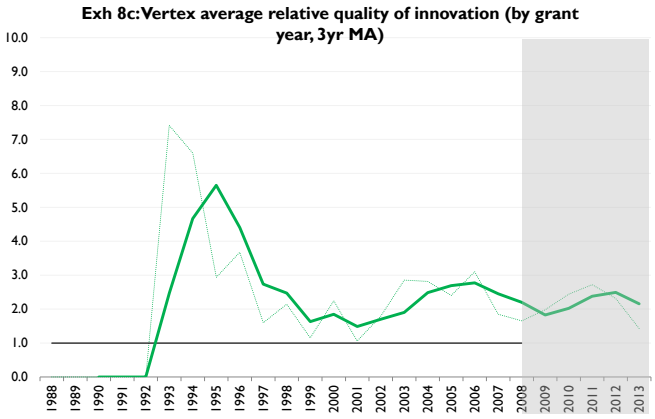


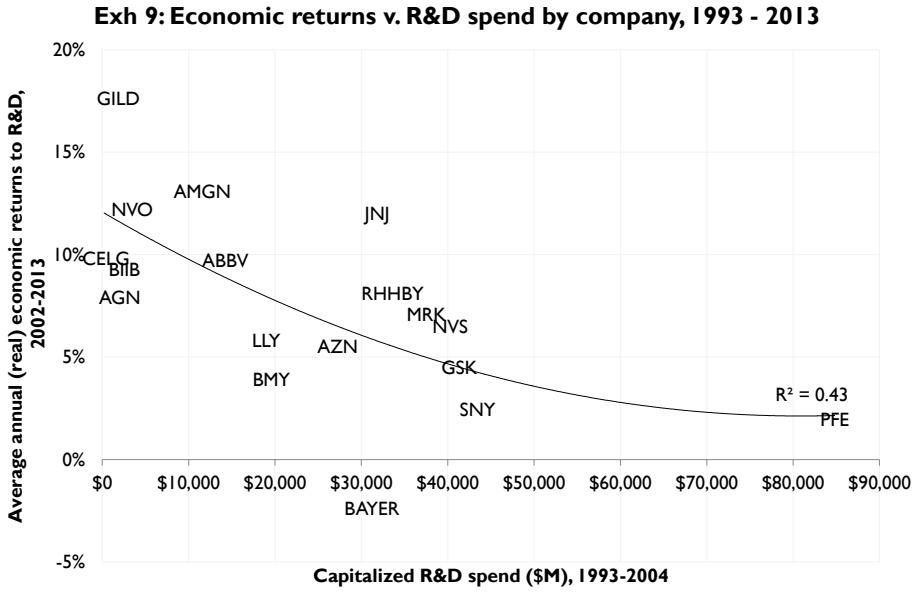
*Until +/- 5 yrs from its Grant date, the ultimate quality/value of a patent is difficult to estimate. Observations from 2008 forward should be viewed with caution

Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

Size

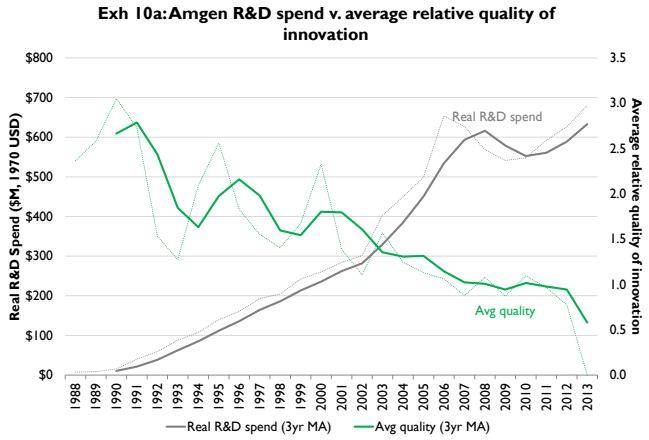
Larger firms tend to have lower R&D productivity than smaller firms; this is true both across firms (larger less productive than smaller) and within firms (a given firm becomes less productive as it grows)

Exhibit 9 demonstrates the principle across firms, comparing cumulative 1993 – 2013 R&D spending for a given company (x-axis) to that company's economic returns to R&D spending (y-axis). **Exhibits 10a** thru **10c** demonstrate the principle within firms for **AMGN, BIIB, and GILD**, respectively. As the real value of each firm's R&D spending grew (grey line, left y-axis), the firm's R&D advantage eroded (average quality of innovation, right y-axis). **VRTX** is the only remaining firm to have kept its R&D quality advantage as it grew (**Exhibit 11**)

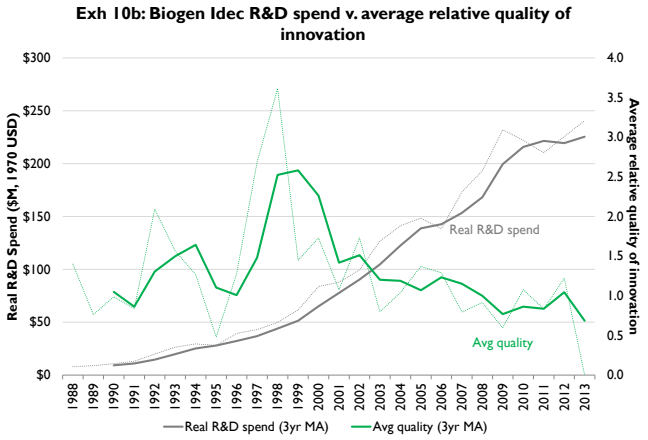


* Excludes ALXN, REGN, SHPG, VRTX which were all non-profitable throughout the majority of the analysis period

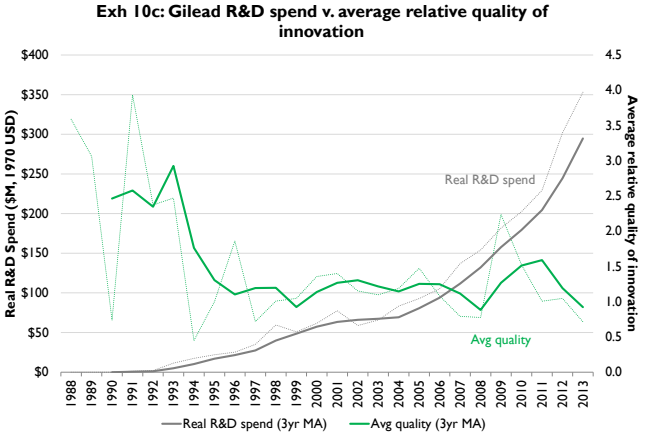
Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions



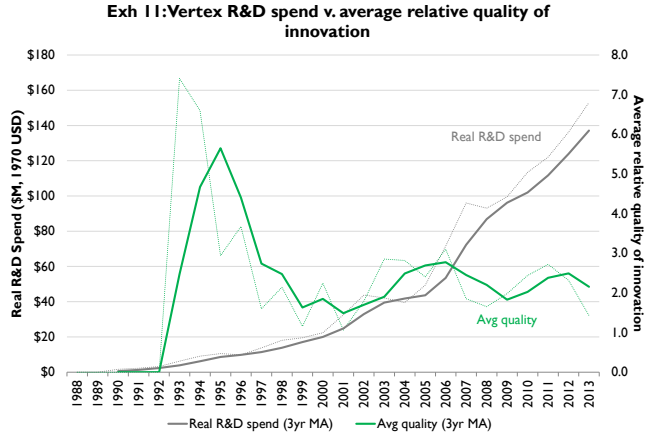
Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions



Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions



Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions



Sources: Bloomberg; AcclaimIP; SSR Health Hidden Pipeline Analysis and assumptions

We appreciate that large size can hardly be described as an unforced error – however allowing (or committing) the behaviors that lead to falling productivity as firms grow is an unforced error. For example, we believe that as firms grow, flows of power, information, and compensation tend to shift from meritocratic (information and money flow to best ideas) toward bureaucratic (information and money flows determined by relatively rigid organizational processes). And, we see a pattern in which innovative breakthroughs form the basis for new companies (at birth, the firm is a great idea seeking capital), who once successful, generate significant cash flows whose primary use is to perpetuate the firm through further discovery (now maturing, the firm becomes capital seeking great ideas). With the exception of **VRTX** (Exhibit 11, again) and **DNA** (not shown), we're unaware of a firm that has maintained a significant R&D productivity advantage during and after a phase (or phases) of significant growth