ENGELBERG CENTER for Health Care Reform at BROOKINGS

State of Biomedical Innovation Conference

The Brookings Institution
June 27, 2012

THE FOUNDRY®
TRANSFORMING CONCEPTS INTO COMPANIES

The Brookings Institution
Mark Deem
June 27, 2012

Metrics to Gauge Health Care Ecosystem

For health care startups the top issues are:

- Financing
- FDA
- Patents
- Burn rate
  - Driven by head count
  - Biggest variable is length of clinical trial

TRANSFORMING CONCEPTS INTO COMPANIES

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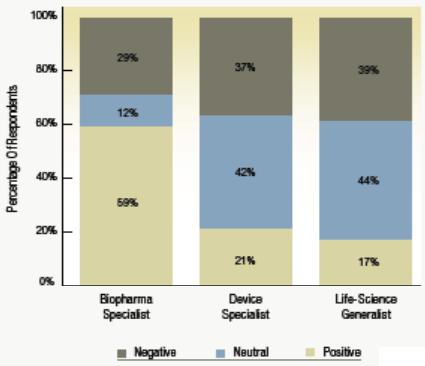
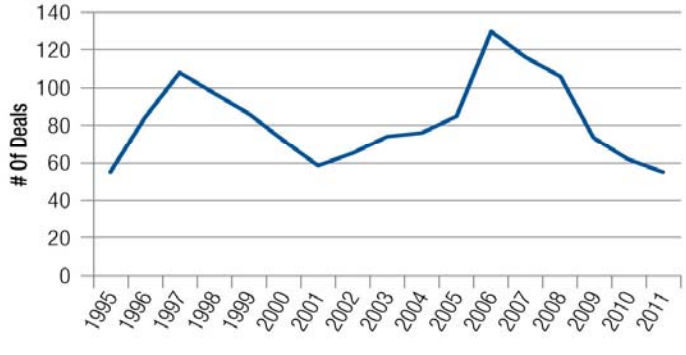
Financing – New Starts and Confidence are Key

Exhibit 1
How Do Investors Feel About The Venture World?



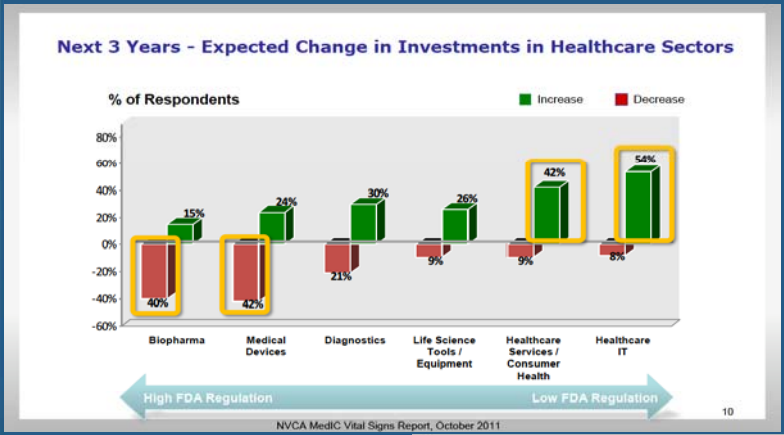
SOURCE: *START-UP*s 2011 Life Science VC Survey

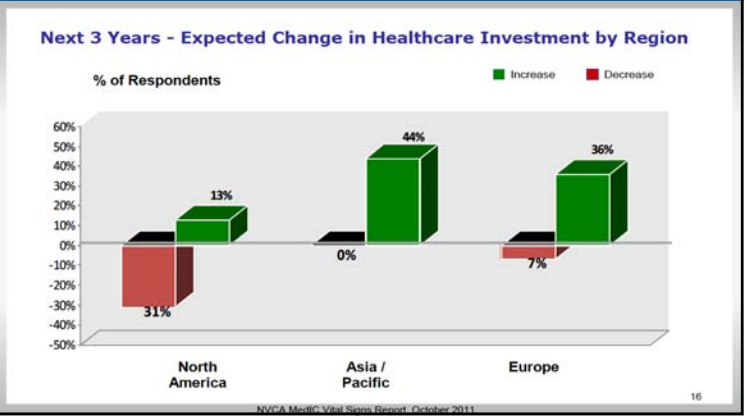
New Medical Device Deals *



* NVCA Money Tree data

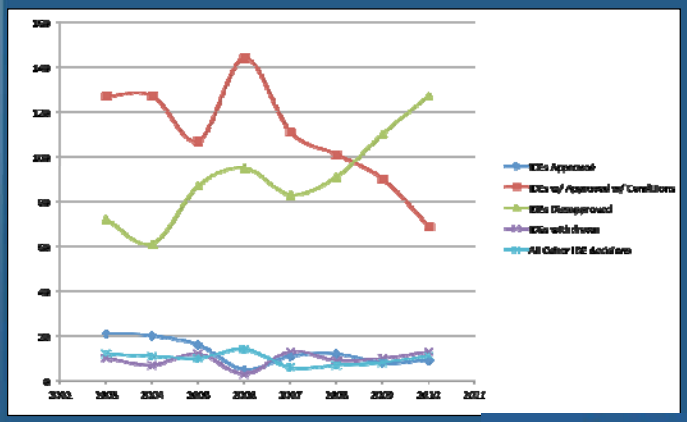
Financing – Forward Looking Expectations





Source: National Venture Capital Association

FDA – IDE & PMA Indicate Innovation Success



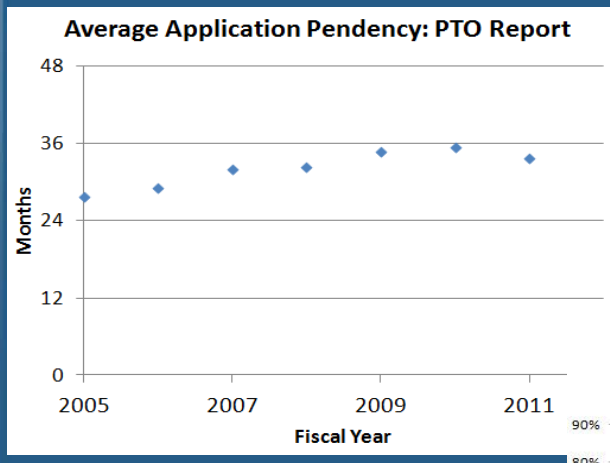
Source: generated from data on www.fda.gov.

PMA data from 2010 not included, and is trending up

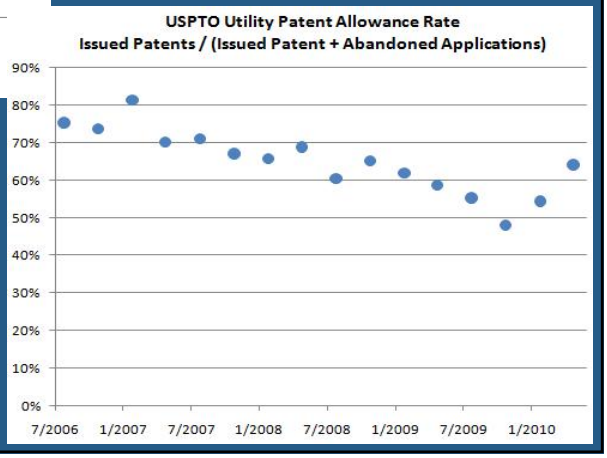
Declining 510(k) clearances and PMAs over last 10 years

*Original PMAs

PTO – Issuance and Pendency



- Pendency decreasing, even as # filings increases
- Quality measures (not shown) key, and are up
- Inflection point = Kappos appointment

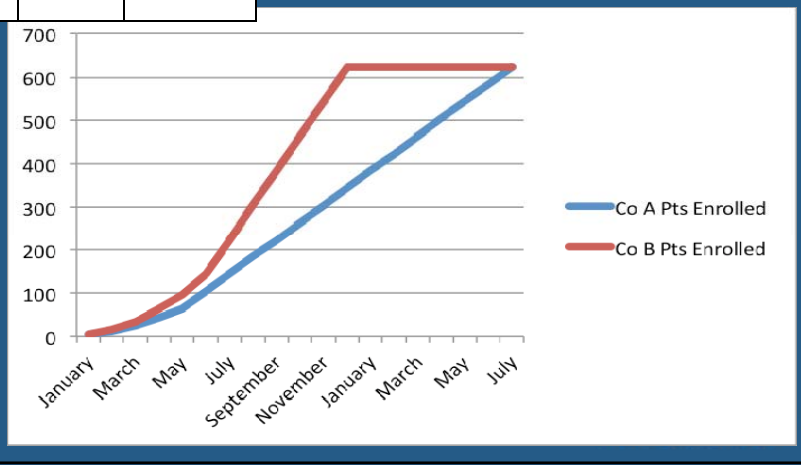


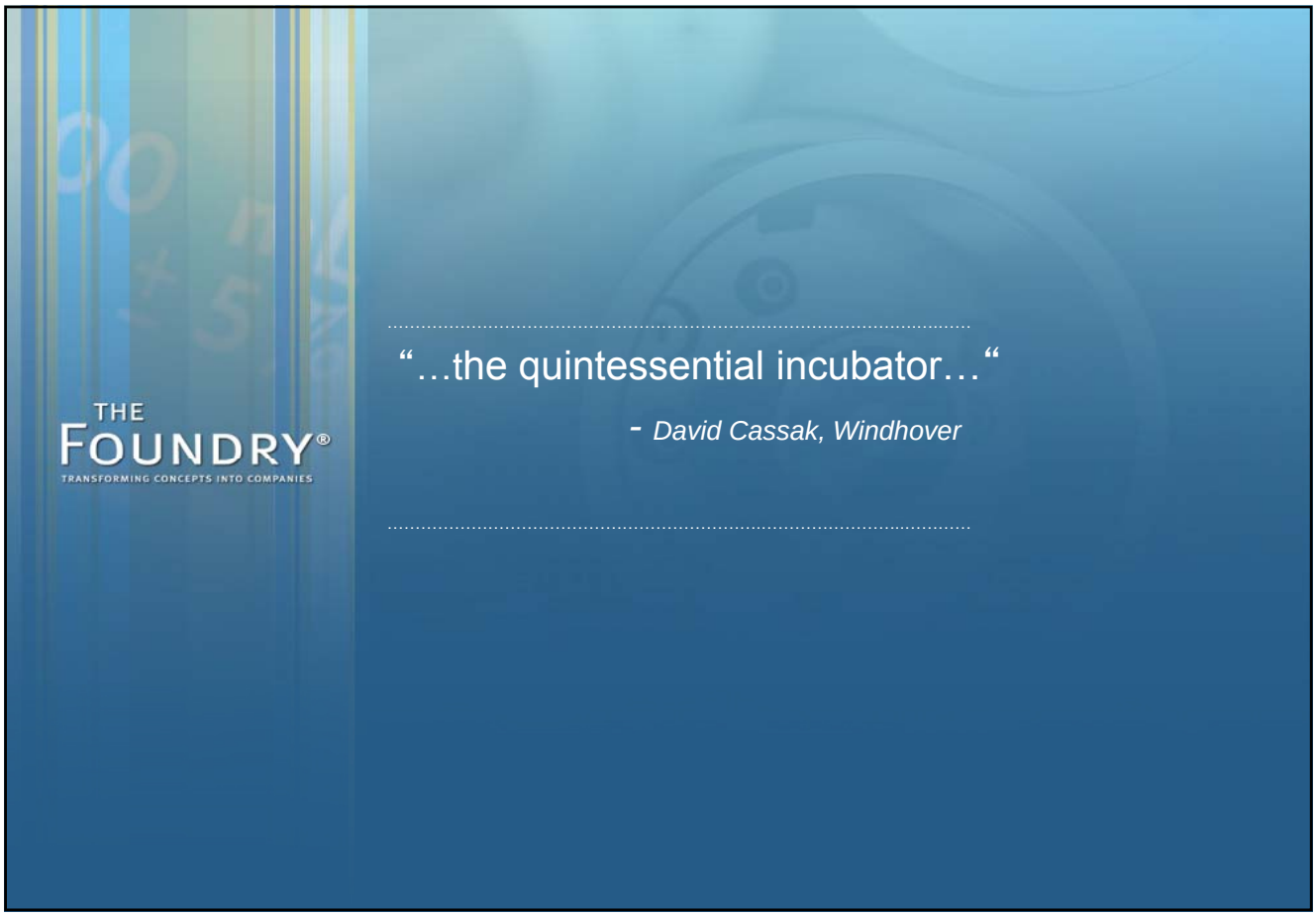
Source: www.uspto.gov

Clinical Trial Efficiency = Life or Death for Startups

Metric	# Sites at Peak	Pt/site/mo at Peak	Burn Rate	Total
Co. A	10	4	$650k	$12.35m
Co B	10	8	$650k	$7.8m

- Enrollment/site is critical
- Every month compounds the miss by company burn rate
- Forces off-milestone fundraising, which can be difficult to impossible today

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TRANSFORMING CONCEPTS INTO COMPANIES
"…the quintessential incubator…"
- David Cassak, Windhover

Measuring The Health of the U.S. Biomedical Innovation Enterprise

A Venture Investor's Perspective

Presentation at the Brookings Institution
"State of Biomedical Innovation" Conference

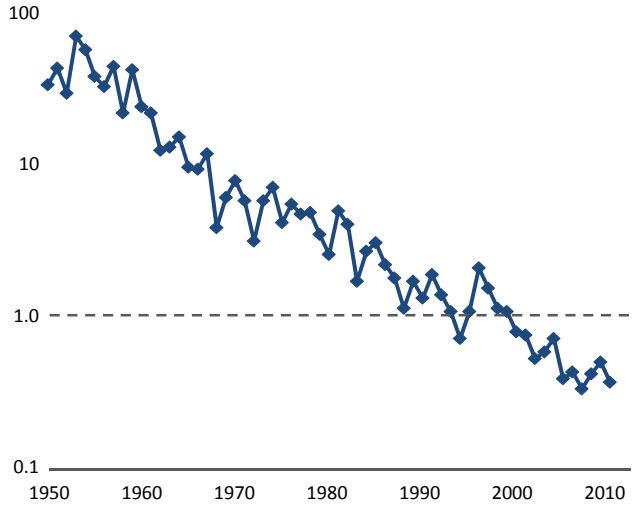
June 27, 2012

Jonathan S. Leff
Warburg Pincus LLC

Biopharma Innovation Is In Crisis

Biopharma R&D Productivity

No. of New Drugs Approved per $BN of R&D Spending



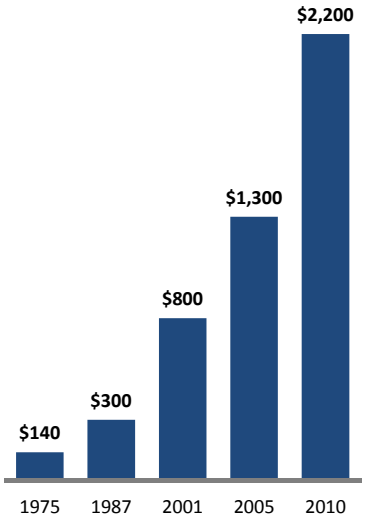
- *"Eroom's Law"*: R&D productivity has roughly halved every 9 years for the last 6 decades!
  - 80x decrease in productivity
- Driven by escalating TIME and COST of drug development
  - Probability of success has remained roughly constant

Source: Scannell et. al, *Nature Reviews Drug Discovery* 11, 191-200 (March 2012).

Time and Cost Are Enemies of Innovation

Estimates of the Cost of Drug Development Over Time

($MM)



Source: DiMasi 2003, 2007, PhRMA, and Bain.

Recent Venture-Backed Drugs: Estimated Total Investment

Brand Name	Indication	Venture-Backed Company	Est. Total Investment ($BN)
Jakafi	Myelofibrosis	Incyte Corp	$1.7
Adcetris	Hodgkin lymphoma	Seattle Genetics	0.8
Dificid	*Clostridium difficile*	Optimer Pharma	0.4
Yervoy	Melanoma	Medarex (BMY)	1.4
Benlysta	Lupus	Human Genome Sciences	3.7
Provenge	Prostate cancer	Dendreon	2.5
Ampyra	Multiple sclerosis	Acorda	0.6
Kalbitor	Angioedema	Dyax Corp	0.5

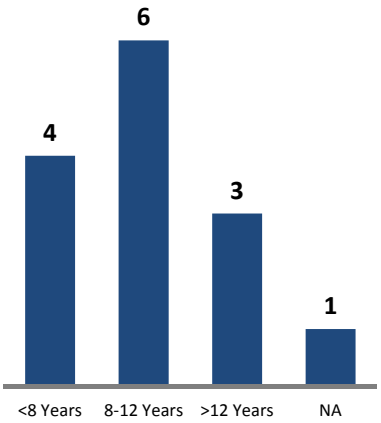
Average: $1.5B
Median: $1.1B

Source: FDA website, Company filings, PharmaProjects, press releases.

Estimated Development Time For 2011 Fast Track Approvals

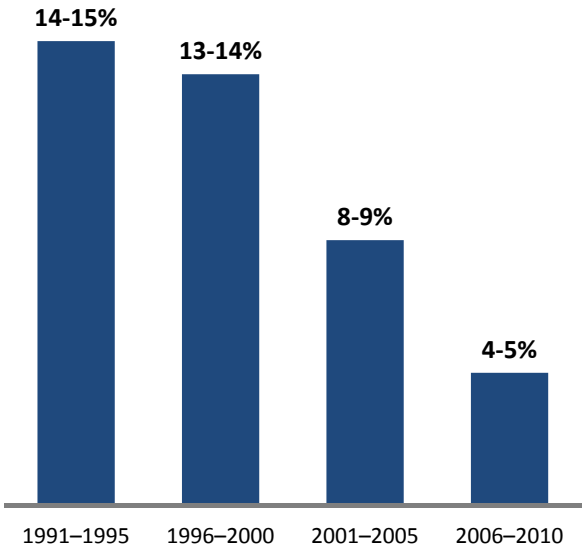
of Drugs

Avg. Years of Development: 11



Return on Investment in Biopharma Innovation Is Declining

Return on R&D Investment for Top 10 Pharmas



Source: McKinsey.

"Pharmaceuticals: Exit Research and Create Value"
– Morgan Stanley, 2010

"At some point, your shareholders and stakeholders demand you have a return on investment in research."
– Ian Reed, CEO of Pfizer, 2011

"[S]ome investors…believe that what we do in R&D is actually value destroying…"
– Chris Viehbacher, CEO of Sanofi, 2011

"I'm absolutely convinced this will be the last generation of R&D spending unless a decent return is generated. The industry will not go forward another ten years spending the money it has been spending unless returns to investors are dramatically greater…or R&D will be cut, and it will be cut significantly."
– David Redfern, Chief Strategy Officer, GlaxoSmithKline, 2011

"At a time when the world desperately needs more medicines for everything from influenza to Alzheimer's disease, our industry is taking too long, we're spending too much, and we're producing far too little."
– John Lechleiter, CEO of Eli Lilly, 2011

Venture Capital Fuels the Development of Most Innovative New Drugs

12 of 14 Fast Track Drugs Approved in 2011 Were Venture-Backed

Name	Indication	Sponsor	Venture-Backed Innovator
Adcetris (brentuximab vedotin)	Hodgkin lymphoma (HL)	Seattle Genetics	Seattle Genetics
Benlysta (belimumab)	Lupus	Human Genome Sciences	Human Genome Sciences
Dificid (fidaxomicin)	Clostridium difficile-associated diarrhea	Optimer Pharma	Optimer Pharma
Erwinaze (asparaginase erwinia chrysanthemi)	Acute Lymphoblastic Leukemia (ALL)	EUSA Pharma	EUSA Pharma
Ferriprox (deferiprone)	Iron overload due to Thalassemia syndrome	ApoPharma	BTG plc
Firazyr (icatibant acetate)	Hereditary angioedema (HAE)	Shire Human Genetic Therapies	Jerini
Incivek (telaprevir)	Chronic hepatitis C	Vertex Pharma	Vertex Pharma
Jakafi (ruxolitinib)	Myelofibrosis	Incyte Corp	Incyte Corp
Victrelis (boceprevir)	Chronic hepatitis C	Schering (Merck)	Corvas
Xalkori (crizotinib)	Non-small cell lung cancer (NSCLC)	Pfizer	Sugen
Yervoy (ipilimumab)	Melanoma	Bristol Myers Squibb	Medarex
Zelboraf (vemurafenib)	Melanoma	Genentech	Plexxikon
Caprelsa (vandetanib)	Medullary thyroid cancer	AstraZeneca	N/A
Nulojix (betacept)	Organ rejection prophylaxis	Bristol Myers Squibb	N/A

Venture Funds Are Not Earning Returns From Biopharma Innovation

Life Sciences Venture Capital Fund Returns

Fund	Year Raised	Rate of Return	Multiple
Essex Woodlands V	2000	8.1%	1.4x
Frazier IV	2000	(3.9%)	0.9x
Perseus-Soros	2001	19.0%	1.7x
Prospect II	2001	4.1%	1.2x
MPM Bio II	2002	N/A	0.8x
SV Intl Life Sciences	2002	N/A	1.3x
TPG Biotech I	2002	4.5%	1.2x
Essex Woodland VI	2003	3.3%	1.2x
Sofinnova VI	2003	(1.5%)	N/A
Frazier V	2004	6.3%	N/A
Aberdare III	2005	(12.0%)	0.7x
Prospect III	2005	(9.3%)	0.7x

Fund	Year Raised	Rate of Return	Multiple
Aisling Capital II	2006	(7.6%)	0.8x
Clarus I	2006	(0.3%)	1.0x
Essex Woodlands VII	2006	1.3%	1.0x
Sofinnova VII	2006	9.6%	N/A
TPG Biotech II	2006	12.0%	1.4x
Health Evolution FOF	2007	(15.8%)	0.7x
Aberdare IV	2008	(17.1)	0.8x
Aisling Capital III	2008	(33.1%)	0.7x
Clarus II	2008	5.5%	1.1x
EssexWoodlands VIII	2008	(8.6%)	0.9x
Health Evolution – Growth	2008	1.9%	1.0x
TPG Biotech III	2008	2.9%	1.0x

Average Rate of Return: (1.4%)
Average Multiple: 1.0x

Source: CalPERS, CalSTRS, CPP, WSIB, and OPERF.

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Essex W [illegible]			0.7x
Sofinnova VI	2003	(1.5%)	N/A
Frazier V	2004	6.3%	N/A
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Aisling Capital II	2006	(7.6%)	0.8x
Clarus I	2006	(0.3%)	1.0x
Essex Woodlands VII	2006	1.3%	1.0x
Sofinnova VII	2006	9.6%	N/A
Clarus II	2008	5.5%	1.1x
EssexWoodlands VIII	2008	(8.6%)	0.9x
Health Evolution – Growth	2008	1.9%	1.0x
TPG Biotech III	2008	2.9%	1.0x

Herbert Stein's Law: "If something cannot go on forever…it will stop."

Average Rate of Return: (1.4%)
Average Multiple: 1.0x

Source: CalPERS, CalSTRS, CPP, WSIB, and OPERF.

Venture Firms Are Pulling Out of Life Sciences Investing

Prospect Venture Partners Unable To Raise New Fund

"Health-care specialists … struggle to find viable models for investing in biotechnology …"
– Dow Jones
(January 2012)

Scale Venture Partners Exits Life Sciences Investing

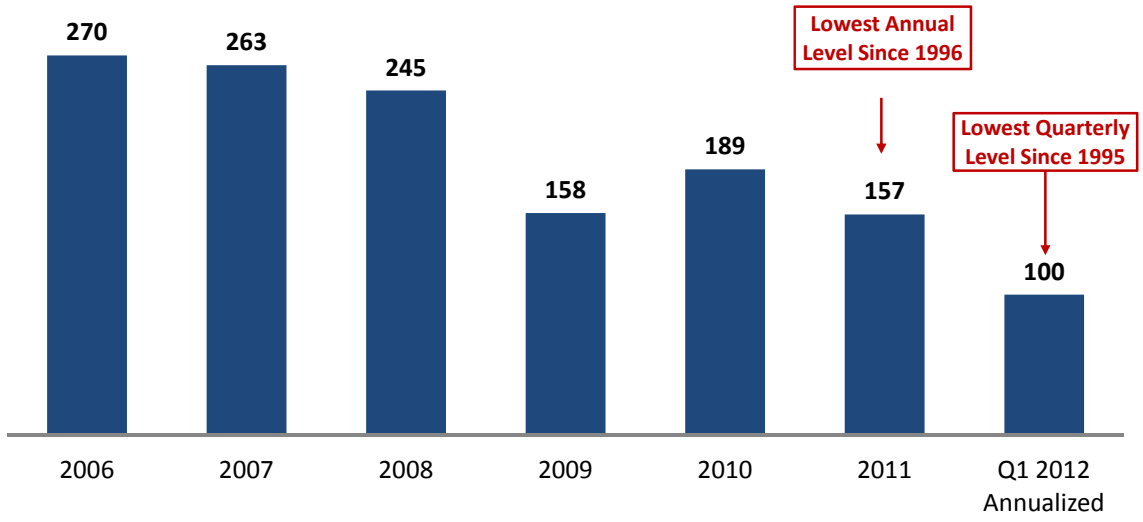
"In the last four years, our companies have filed 7 NDA's – something we are proud of. Unfortunately, they took longer and used more capital than planned from the start."
– Kate Mitchell, Scale Venture Partners
(Scale Venture Partners Blog, November 2011)

Providers of Capital ("Limited Partners" or "LPs") Questioning The Merits of Life Sciences Investing

"The more sophisticated LPs are concerned with the regulatory environment and the ever-increasing cost of clinical trials. The cost burden has gone no place but up."
– Michael Powell, Ph.D., Sofinnova Ventures
(BioCentury Interview - October 2011)

Venture Capital Investment In Life Sciences Innovation Is Under Serious Pressure…

Life Sciences Companies First-Time Fundings



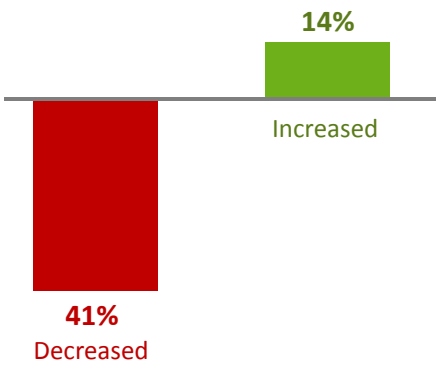
Source: NVCA/PWC MoneyTree report.

…And Venture Capitalists Expect to Continue to Pull Back

NVCA Survey of Life Sciences Venture Capital Investors (October 2011)

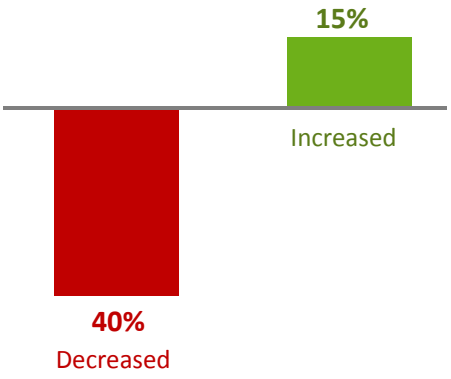
Past 3 Years Change in Biopharma Investment

% of Respondents



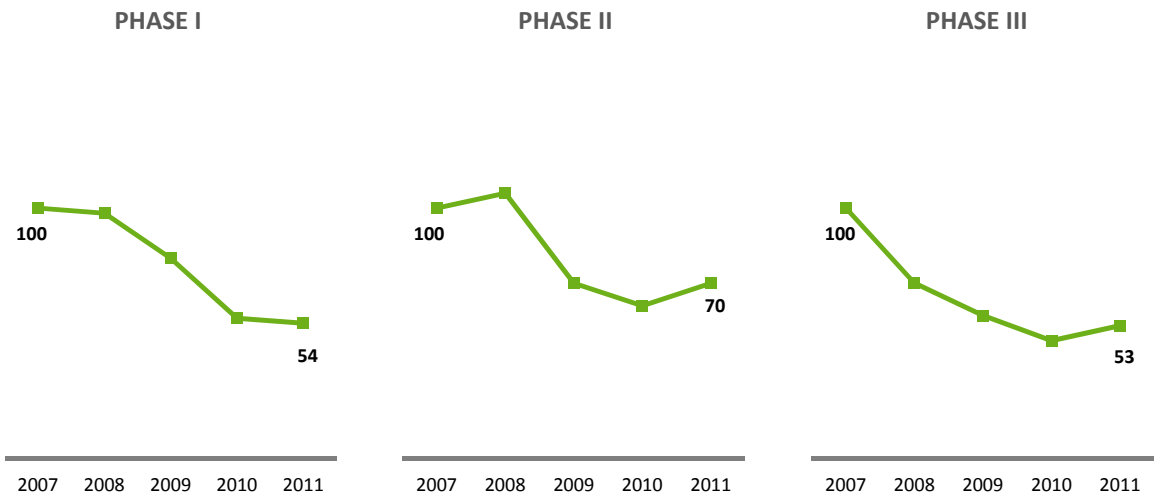
Next 3 Years Expected Change in Biopharma Investment

% of Respondents



Reduced Investment Appears To Be Taking A Toll on New Clinical Trial Starts

Indexed Trend in New Drugs Entering Each Phase of Development



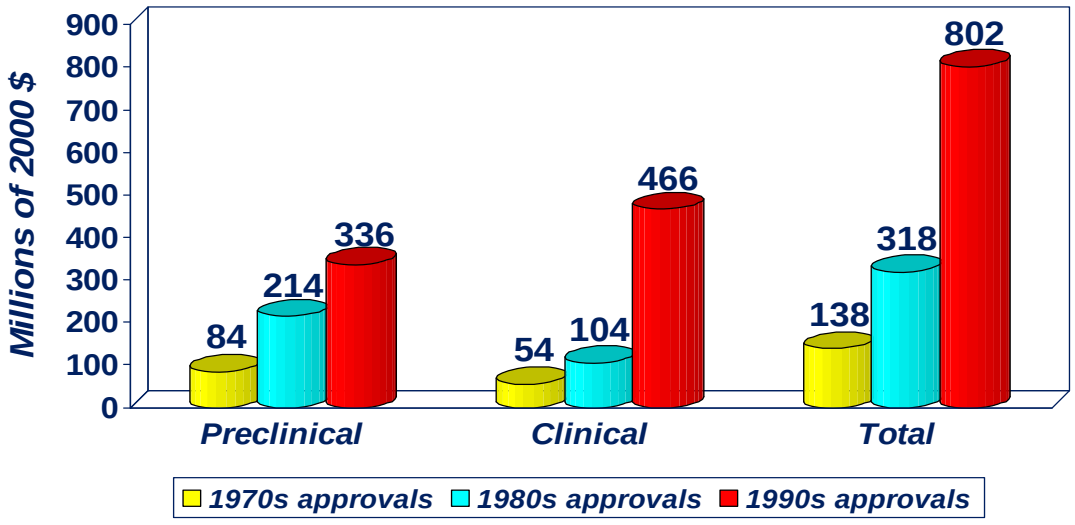
Source: CMR 2012 Pharmaceutical R&D Fact Book, Thomson Reuters.

Annual State of Biomedical Innovation

Henry Grabowski
Duke University

Brookings Institution Conference
June 27, 2012

Trends in Fully Allocated Capitalized Cost per Approved Drug

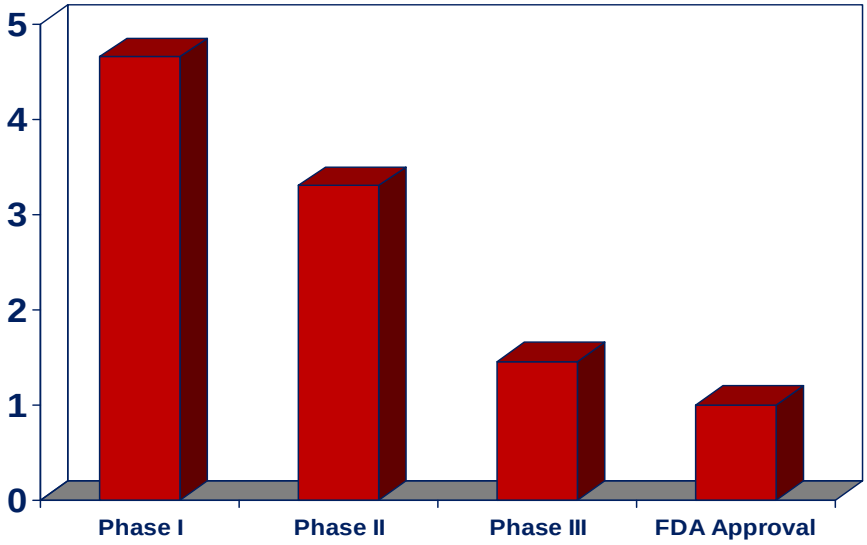


Source: DiMasi et al., J Health Economics 2003;22(2):151-185

Why is R&D Process for New Drugs so Long and Costly?

- Scientific, regulatory, and commercial uncertainties
- Management of the R&D process is highly variable
- Multiple testing phases involving 1000s of subjects
- Most new drug candidates fail to reach the market

Number of Drug Candidates Required to Achieve One Approved Compound



Source: DiMasi et al., *J Health Economics* 2003;22(2):151-185

R&D Costs per New Drug Approval Determinant Factors - Clinical Phase

- Probability of success
- Number of subjects
- Clinical trial complexity
- Input prices
- Clinical trial length
- Cost of Capital

Quality Output Measures of NMEs

- Priority versus standard FDA approvals
- First in class <new mechanism of action>
- Significant advance in existing class
- Consensus or global NMEs
- Weighting FDA approvals by sales
  - patent citations
  - medical articles, citations, etc.

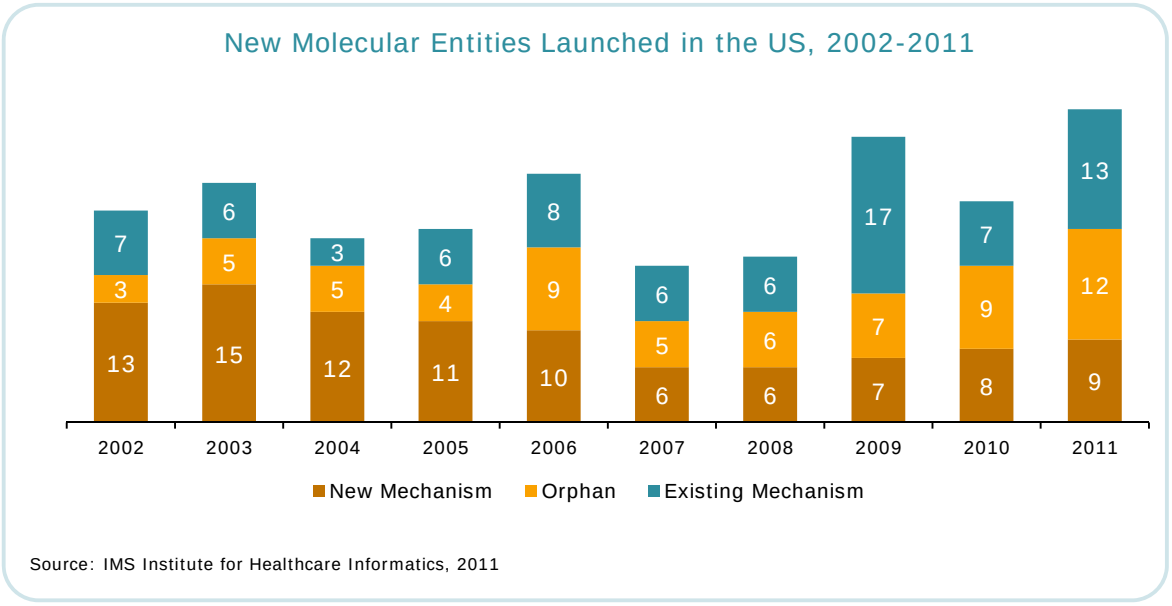
IMS INSTITUTE FOR HEALTHCARE INFORMATICS

State of Biomedical Innovation Conference

Murray Aitken
Executive Director

TRANSFORMATIONS IN DISEASE TREATMENT

More new medicines were launched in 2011 than in the past decade



Source: IMS Institute for Healthcare Informatics, 2011

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Audience Q&A