

A Venture Capital Perspective

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**Innovation
Patient Benefit
Superior Returns**

Content:

- *Brief Overview of NVF*
- *Venture Capital Primer*
- *Impact of VC on US Economy (disclosure: NVCA lens)*
- *State of Healthcare Venture Capital*
- *VC Market Challenges*
- *Incentives & Healthcare*
- *Challenges for VC Backed Companies Pursuing Military Priorities*

Venture Imp

***Brief Overview of the Novartis
Venture Funds***

Novartis Venture Fund – Innovative and Successful

■ A Decade of Success

- In 14 years developed into the leading corporate venture capital firm
- CoC multiple and IRR based on all realized exits and losses in top quartile of VC benchmark
- Investment Focus: Strategic to the health care industry
- NVF reputation viewed as progressive & forward thinking:
 - Two capital choices – Venture Fund and Option Fund
 - Independent decision making

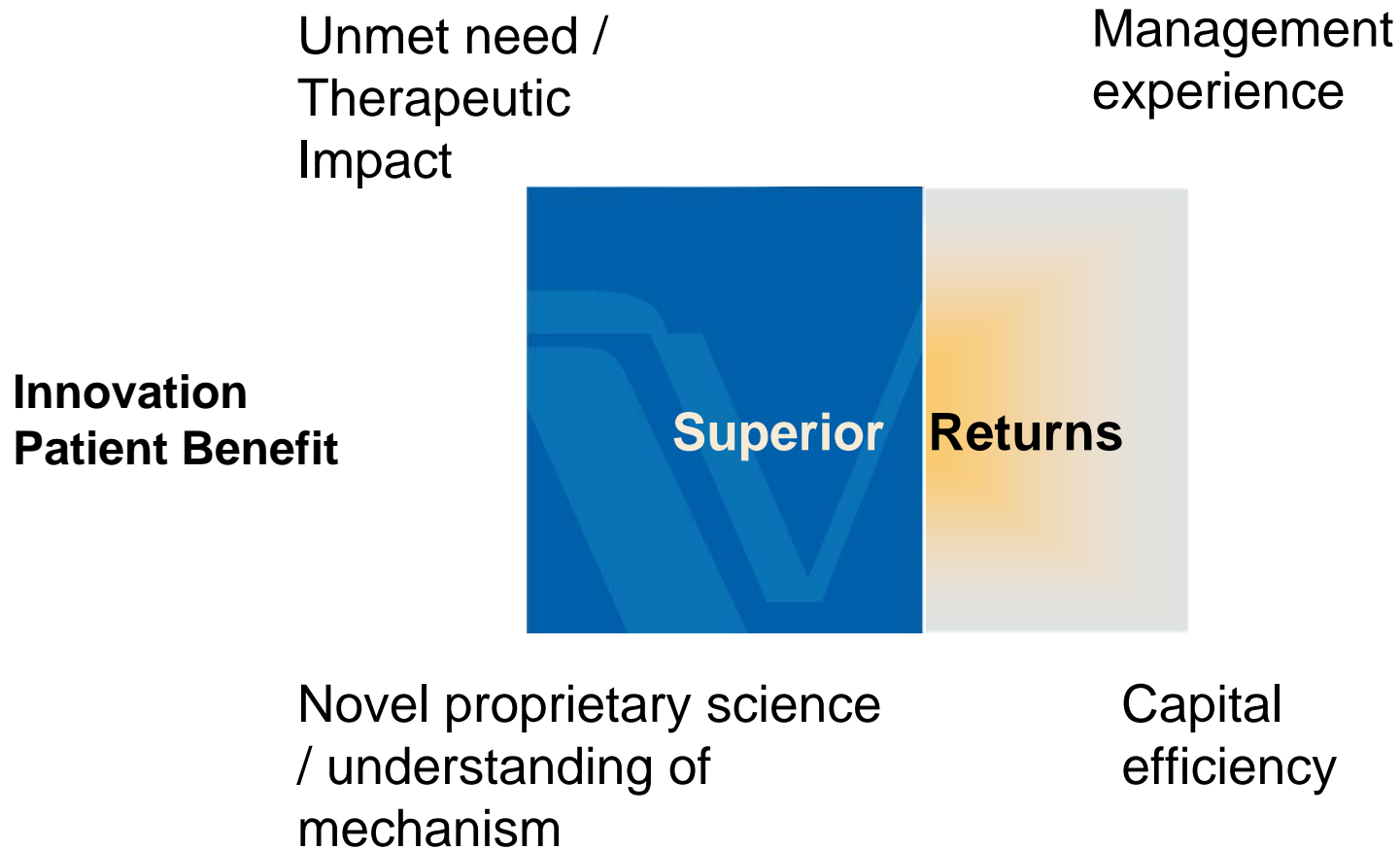
■ Novartis Venture Fund portfolio:

- 3 funds: NVF, NOF, Korea fund
- ~65 private companies
- 7 LPs commitments
- ~\$750M USD Capital Base
- ~\$15-20M USD per investment
- 8-12 new investments / year
- 40+ portfolio company board seats
- Experienced team based in Cambridge and Basel

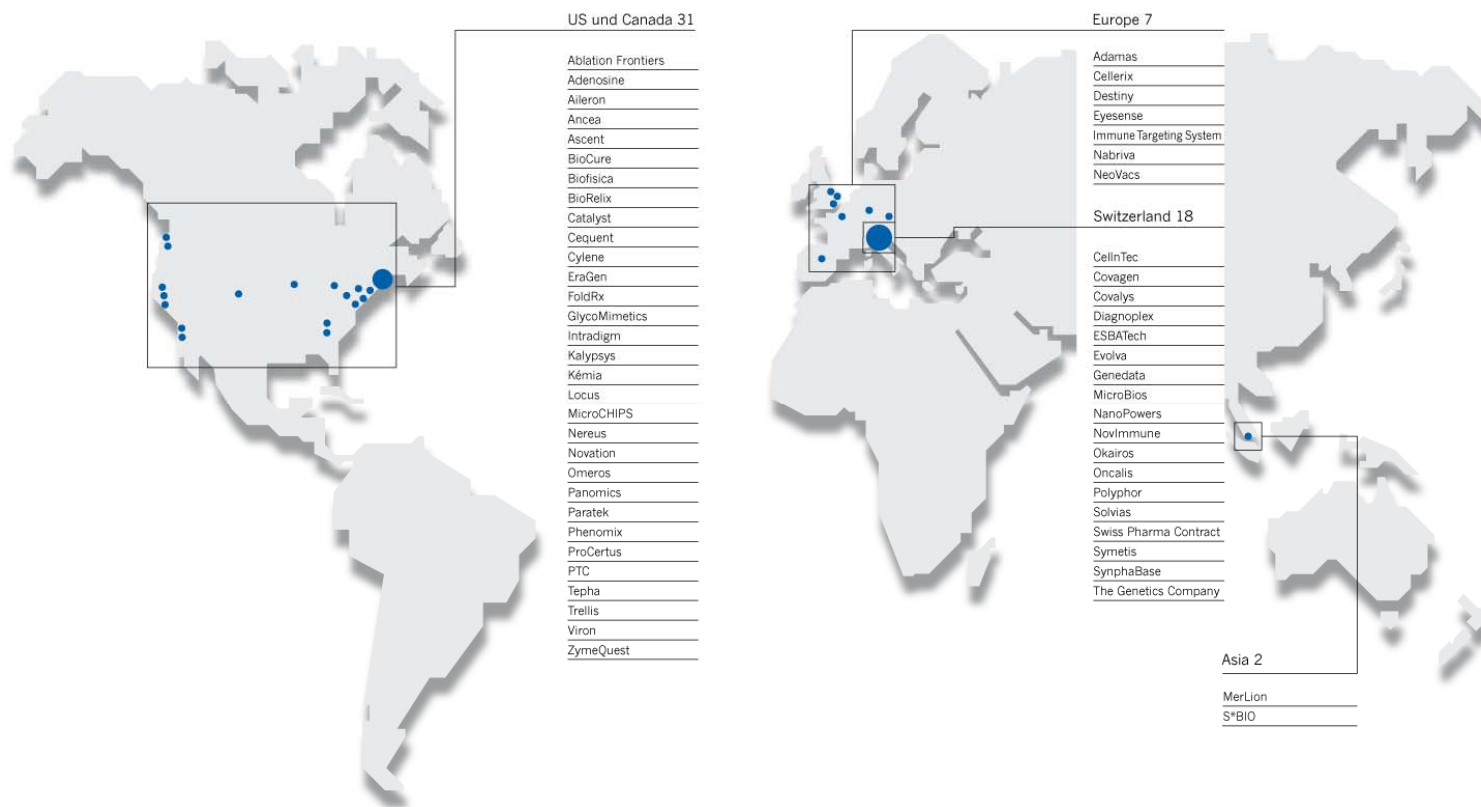
NVF - Summary

- **NVF Mission:**
 - Investing in innovative life science companies for patient benefit, creating attractive returns for entrepreneurs and investors
- **Investment philosophy:**
 - Strategic to the entire health-care industry (therapeutics, diagnostics, medical devices)
- **Strong, experienced team:**
 - Proven track record on financial performance and operational support (board level) for portfolio companies
- **Governance structure :**
 - Two independent Advisory Boards
- **Market position:**
 - Largest corporate biotech VC, with strong network and influence in VC and biotech industry

NVF Investment Criteria



Geographic Distribution of Companies



Key Factors for Successful Investments

- Team continuity and institutional learning critical to long term success
- Board representation is important to influence company development
- Relationships / reputation with entrepreneurs and investors are invaluable to access deals
- Syndicate quality and financial reserves enable strategic and operational flexibility
- Focus on innovation with strong patient / physician benefit drive attractiveness of business
- Capital efficiency via operational and financial discipline determine return
- Start investment with the end in mind

Venture Capital Primer

What is Venture Capital?

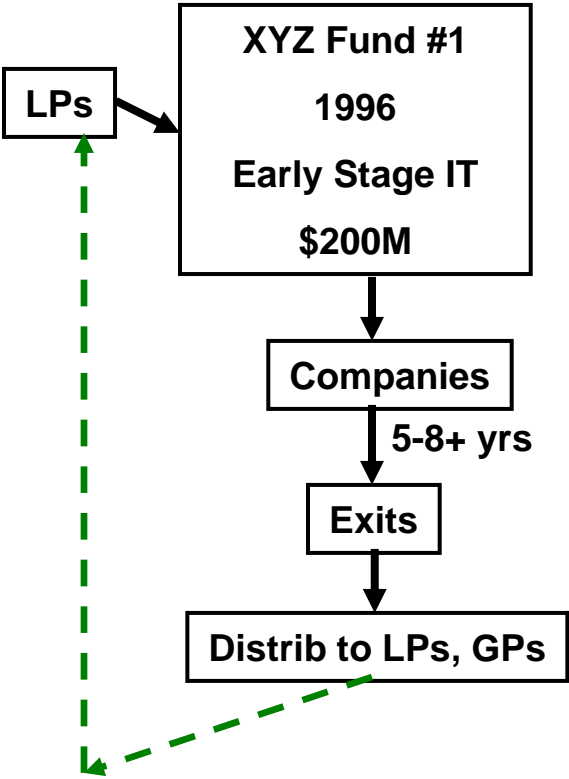
- Venture capital is invested alongside management in private start-up companies operating in innovative industries.
 - Information Technology
 - Life Sciences
 - Clean Technology
- Venture funds are capitalized by institutional investors and the VCs themselves.
 - Pension funds
 - Endowments
 - Foundations
 - Corporations
 - Family offices, wealthy individuals
- The goal of a venture investment is to build a company until it can stand on its own as a public entity or be acquired as part of a larger organization.

Sources of Capital: Many Options to Choose From

- Entrepreneur personal funds
- “Friends and family”
- Personal credit card and other borrowings
- Angel investors
- Venture capital
- Corporate direct investment
- Venture leasing
- Mezzanine financing
- Merger and acquisition
- Initial public offering
- Secondary/follow-on public offering
- Private placements – debt & equity
- Buyout/acquisition financing
- Corporate debt

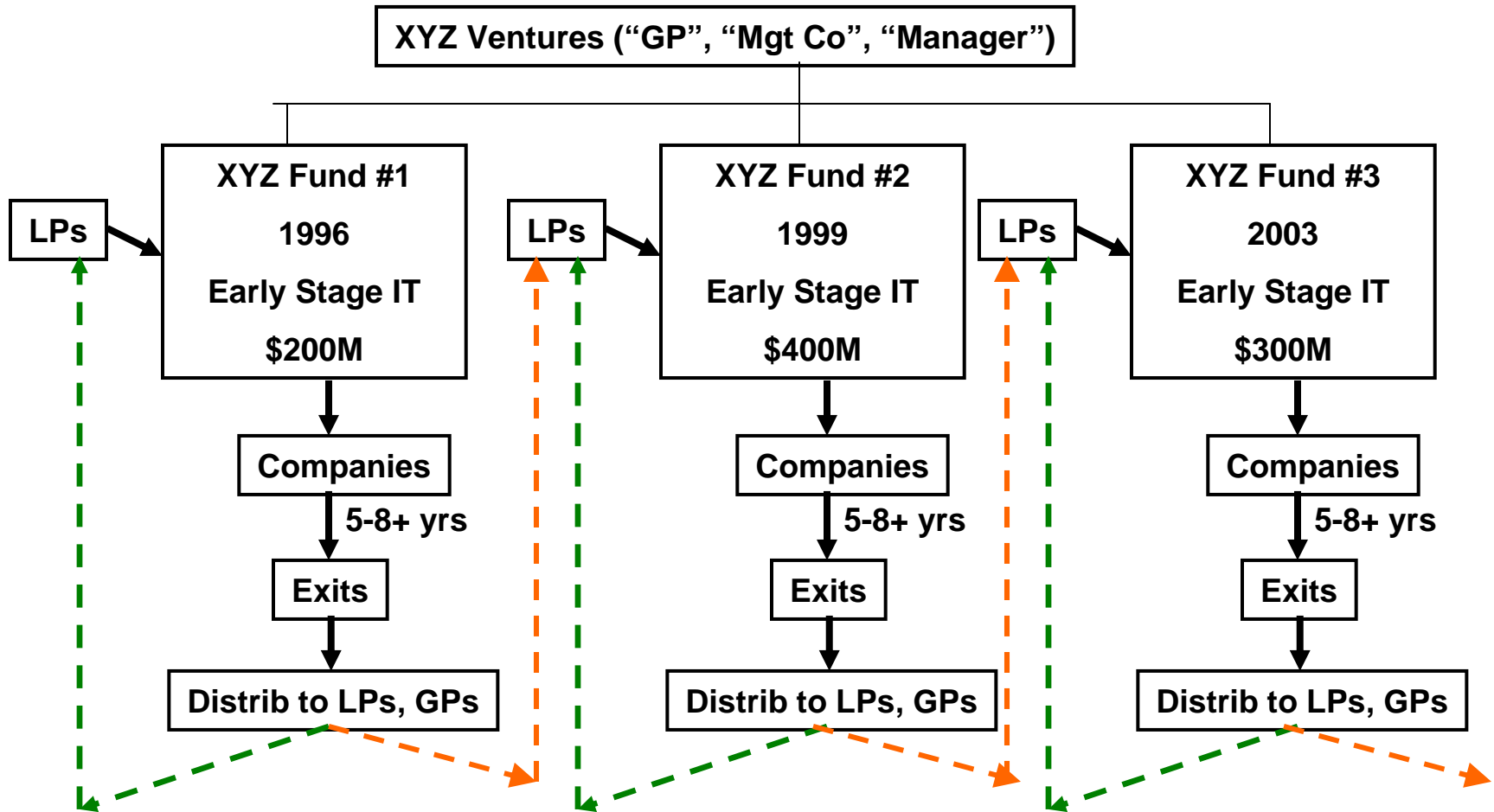
VC Ecosystem

XYZ Ventures (“GP”, “Mgt Co”, “Manager”)



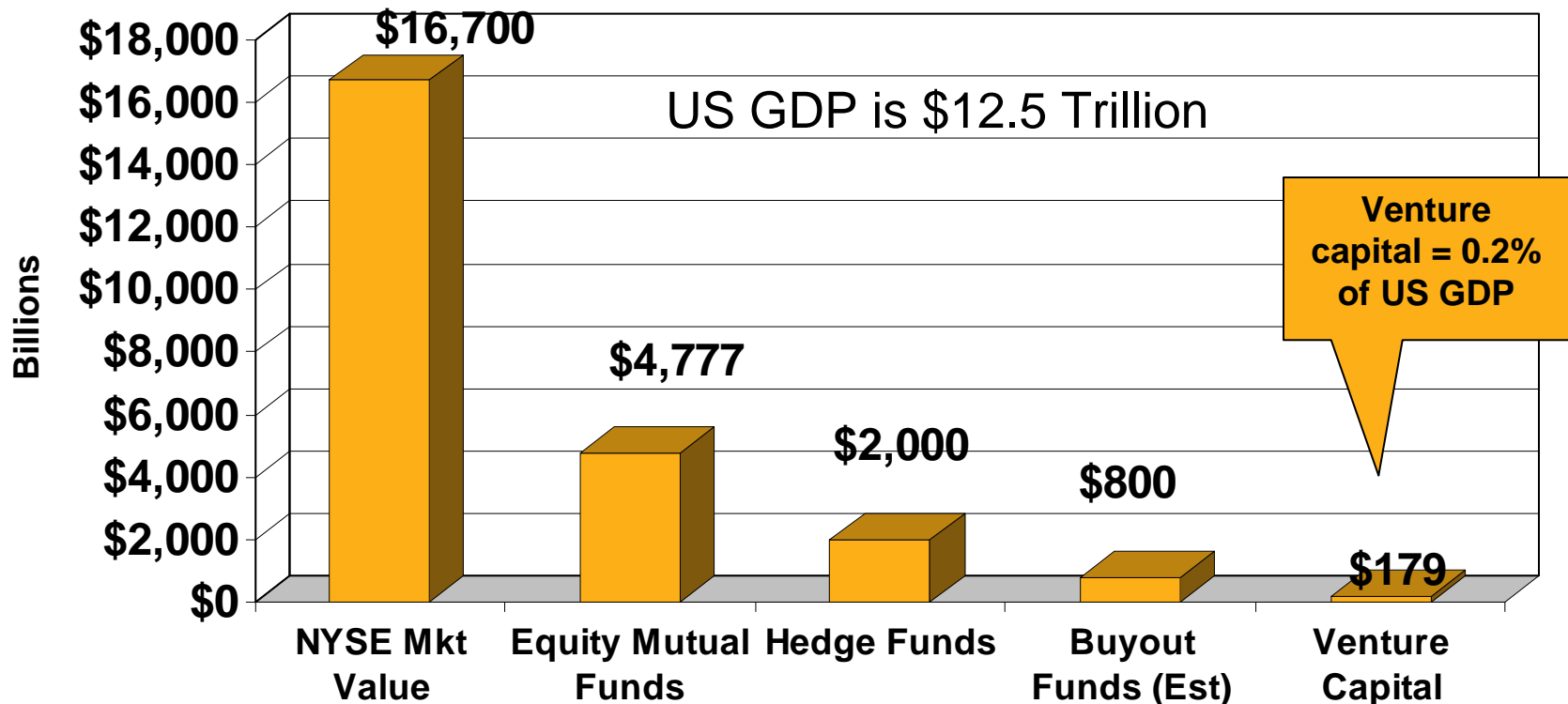
Source: NVCA

VC Ecosystem – One Venture Firm



US Venture Capital Investment in Perspective circa 2009

Assets Under Management



Venture Impact

The Economic Impact of Venture Capital on the US Economy ...

More than deals and exits

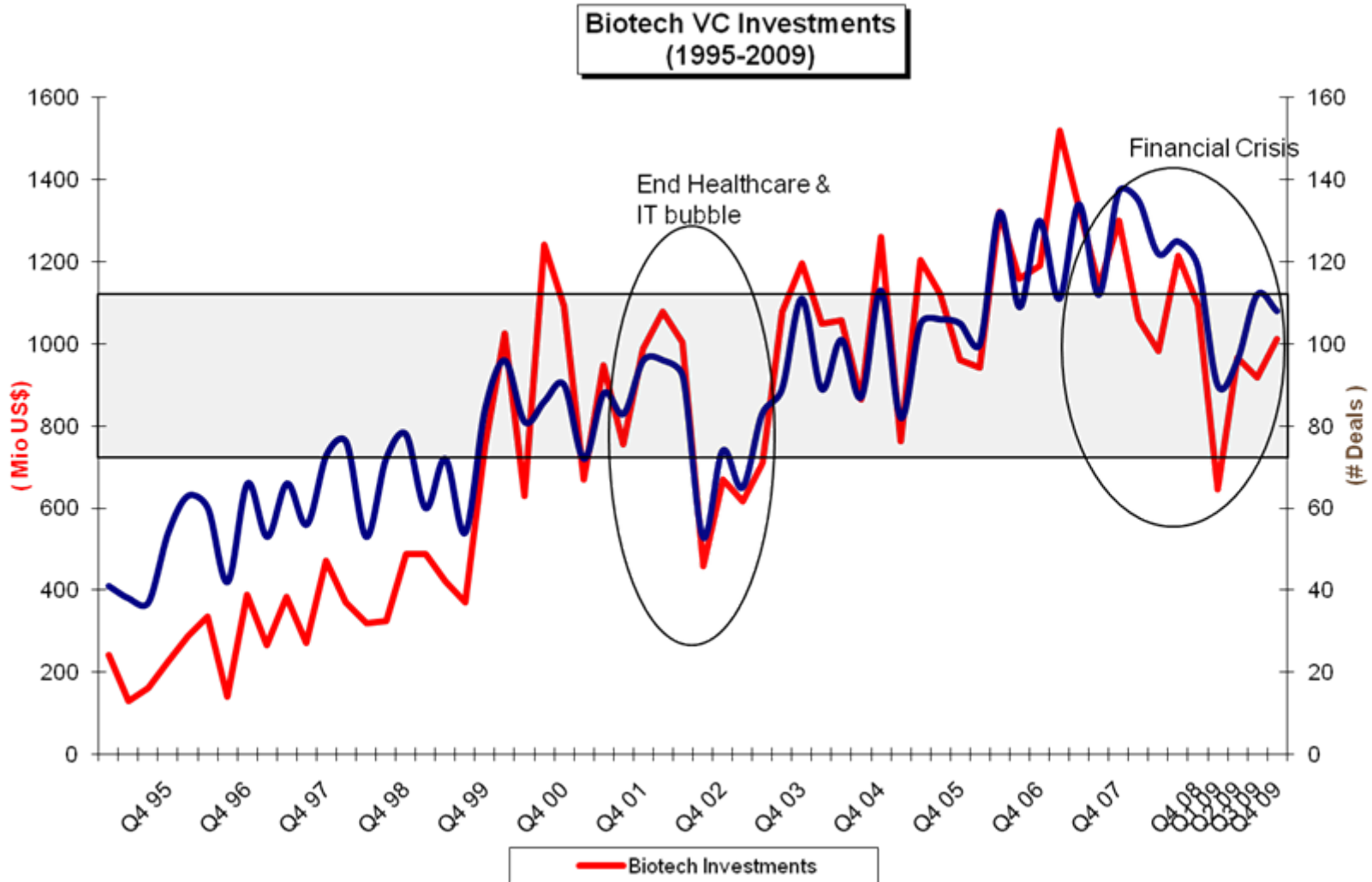
So how do we measure the results?

Global Insight Study

- In 2008, venture backed companies:
 - Provided over 12 million US jobs
 - Had sales of \$2.9 trillion
 - Represents 20.5% of GDP
 - Still dominated venture-created sectors
 - 74% of telecommunications jobs
 - 81% of software jobs
 - 55% of semiconductor revenue
 - 67% of electronics/instrumentation revenue

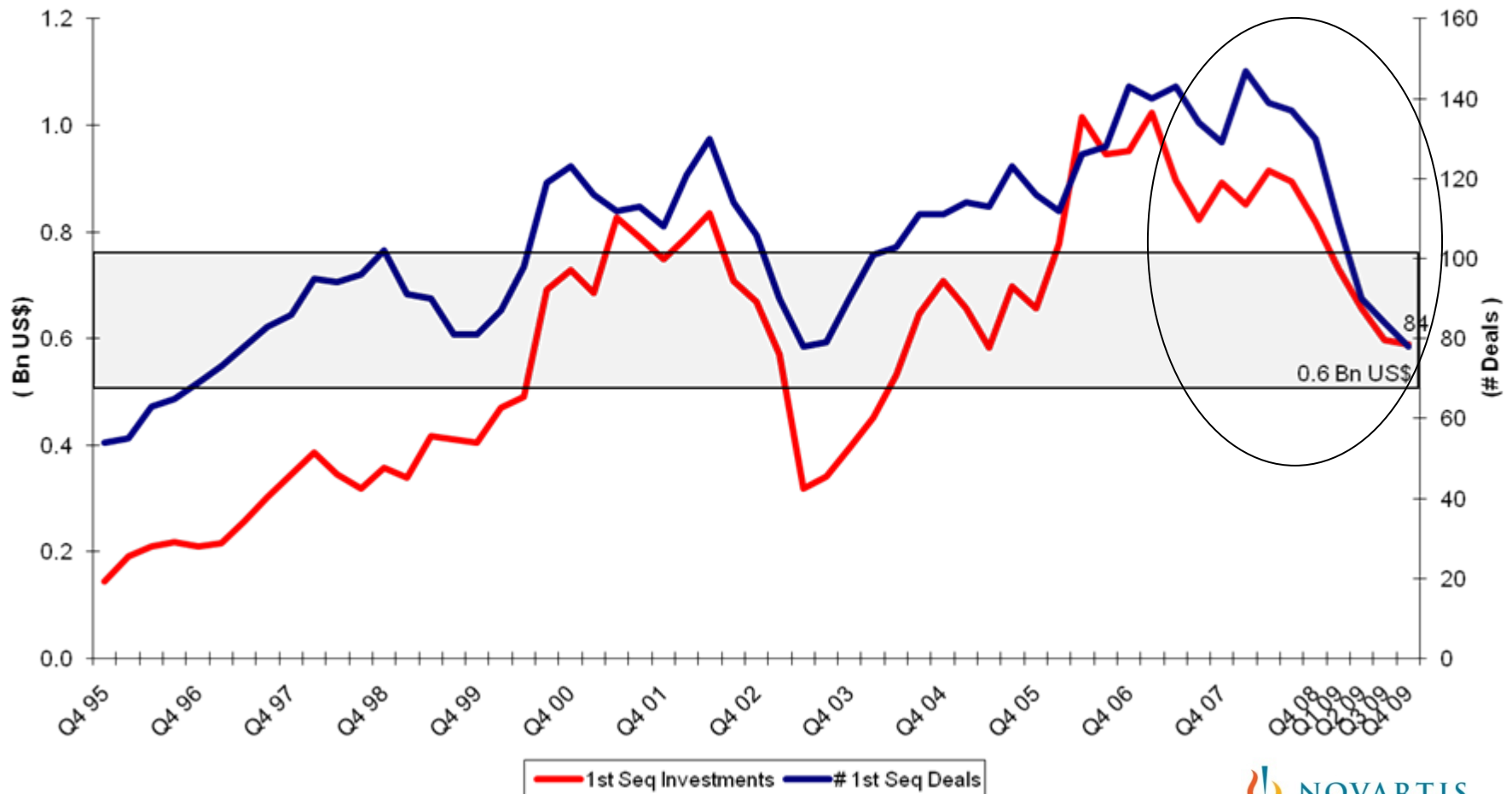
State of Healthcare Venture Capital

Overview: Biotech Investments



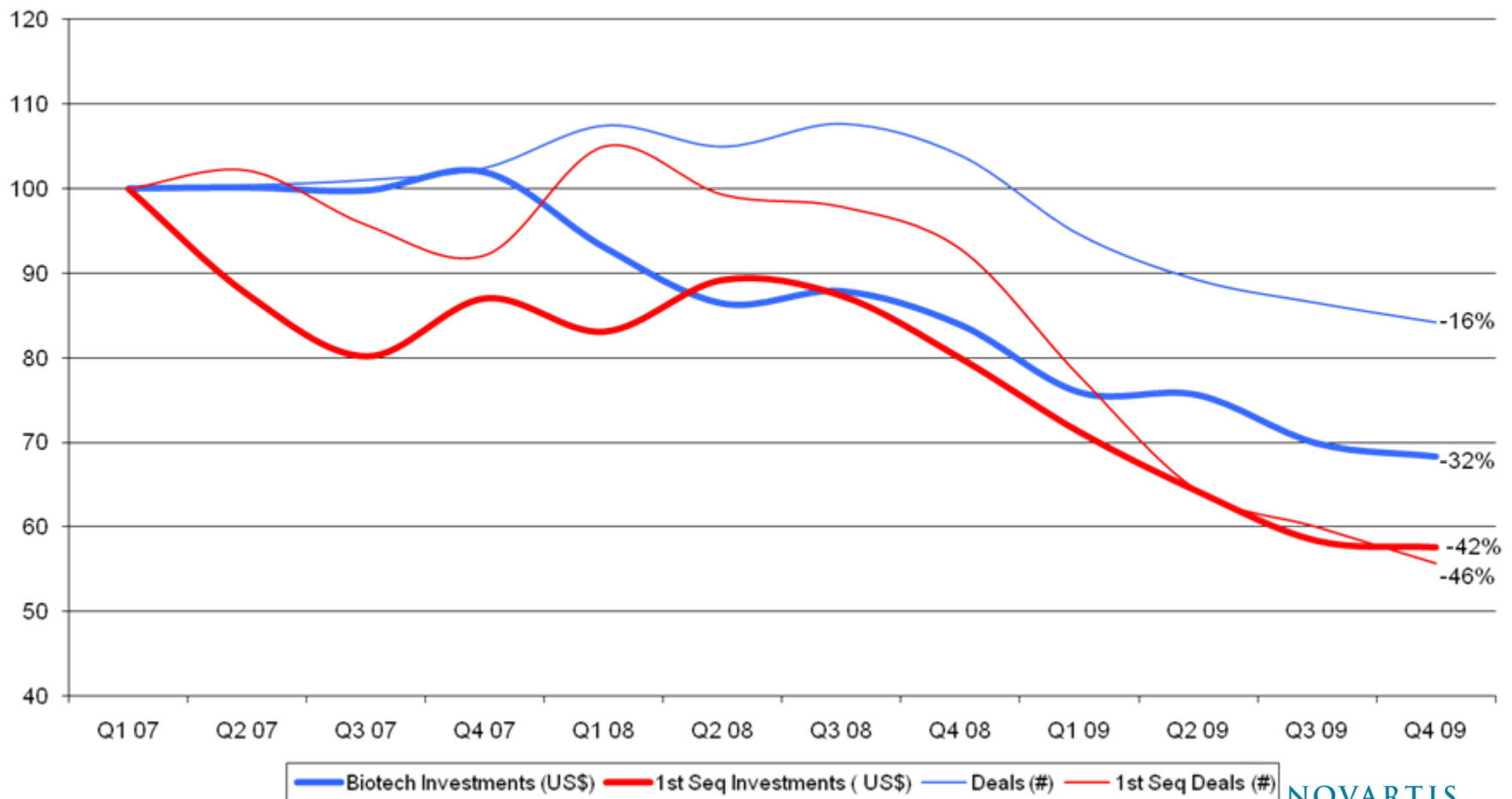
Biotech Investments: New Investments Down

Biotech 1st Sequence Investments MAT
(1995-2009)

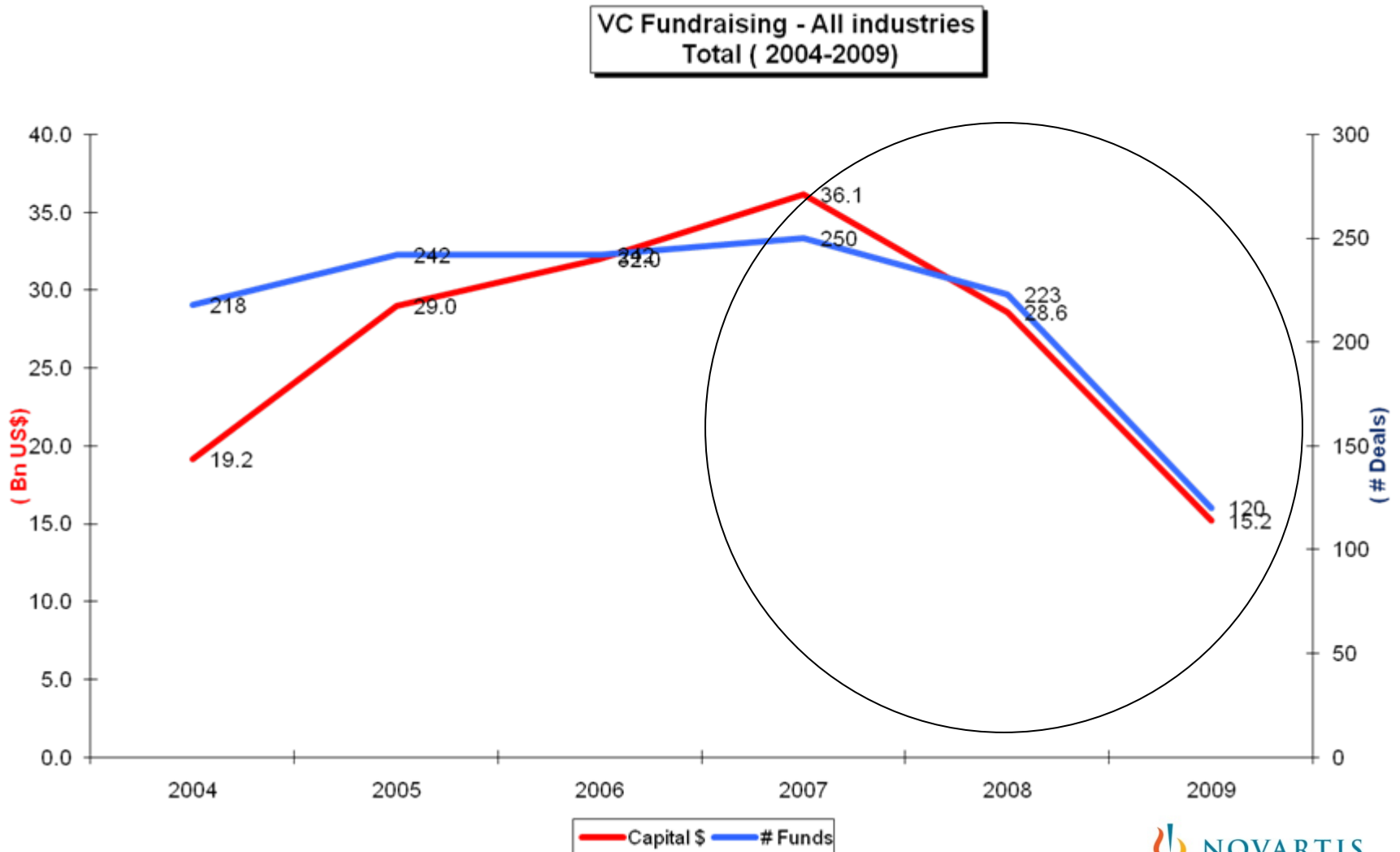


Biotech Investments: Continued Decline

Total vs. 1st Sequence Biotech VC Investments
(2007-2009)



VC Funding Raising Declined 2008/09



Venture Capital Investment is Productive ...

- For each VC dollar invested from 1970-2001, there was \$9.88 in US revenue during 2008 yielded
- For every \$24,564 of venture capital invested in 1970-2001, there was one job in the year 2008
- Note these ratios are based on investment through 2001 (\$296B) because investment after that time has likely had little effect on jobs and revenues. If investment 1970-2008 (\$456.2B) is used, the ratios would be \$6.28 and \$38,606 respectively

Current VC Biotech Market Challenges

- **The market environment is harsh:**
 - **Exits are limited**
 - Biotech IPO market is weak
 - Fewer M&A exits to big pharma as pharma attention & bandwidth is consumer by merger & integration issues
 - (e.g. Pfizer/Wyeth, Merck/Schering, Merck AG/Serono, Roche/Genentech, Novartis/Alcon, AstraZeneca/MedImmune, J&J/Crucell)
 - Consequently, while M&A still attractive more deals tend to get structured with up-fronts reduced and staggered milestones
 - **Cash needs are higher, and operational expertise greater**
 - Result is higher funding requirement of portfolio companies and delayed cash returns, reducing both CoC and IRR
 - Need to be an active investor to drive focus and keeping companies funded is paramount

Current Challenges in the VC Biotech Market

- **The VC world is becoming more selective and competitive:**
 - New investors are selective and diligence levels have grown
 - Bigger trenched financing rounds and more inside-led syndicates
 - Increased competition for the best/risk-mitigated companies
 - VC players without critical mass (man power and \$) get squeezed out of deals

In Response to Challenges... Investors are Defending Their Own First

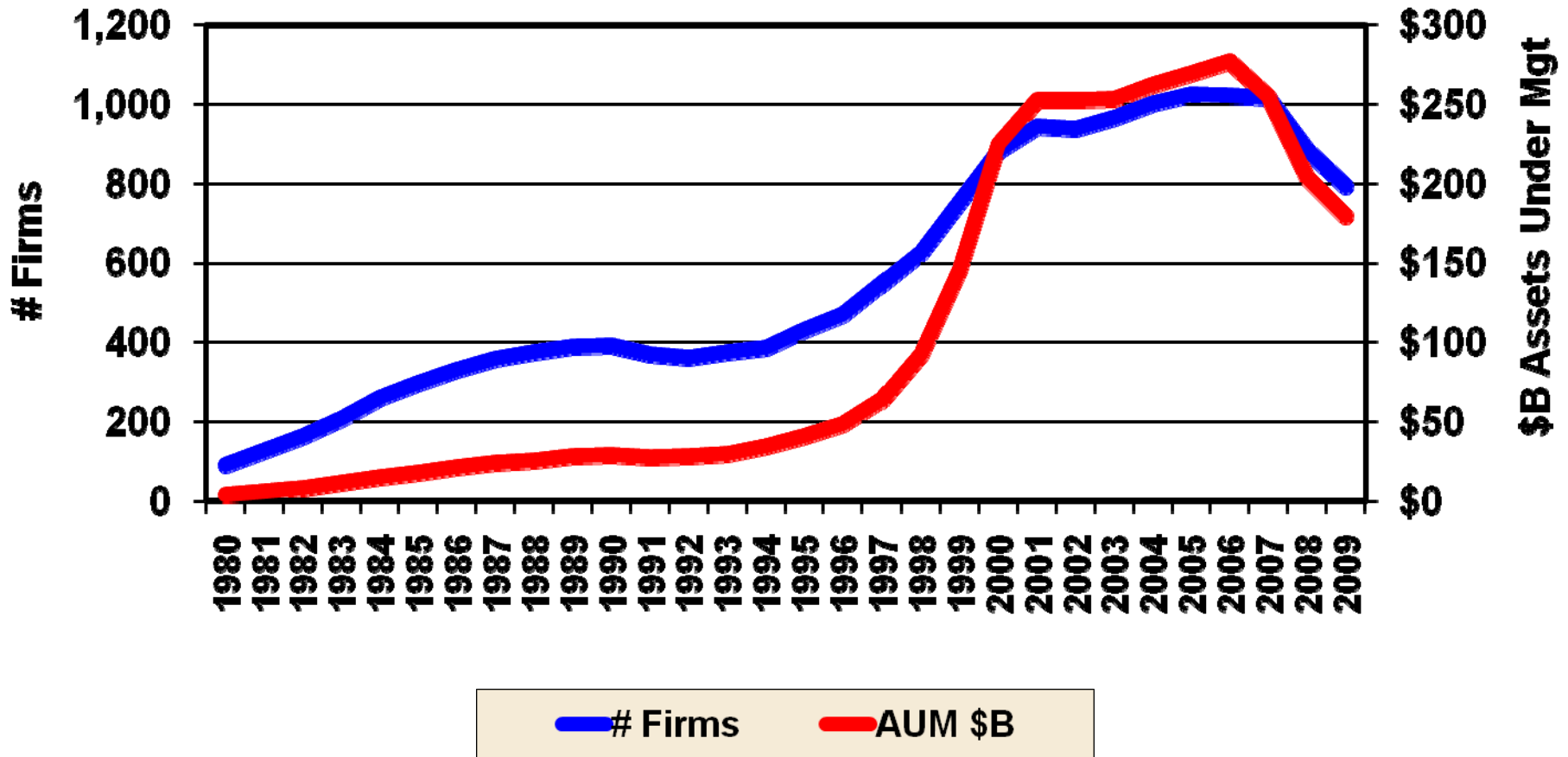
- More capital constrained
 - Fewer funds being raised - LP community limiting venture allocations
 - Funds able to be raised are smaller
 - Funds re-allocating capital reserves to existing companies

But there is a silver lining...

- **For VCs with cash remaining, good quality deal flow is high**
- **Pharma needs deals for their pipeline**
 - Once the consolidation wave settles, opportunities for attractive returns to investors may increase

Fundraising & Resources

AUM Peaked at \$276B, Now \$179B; # Firms Down from 1023 Peak to 794

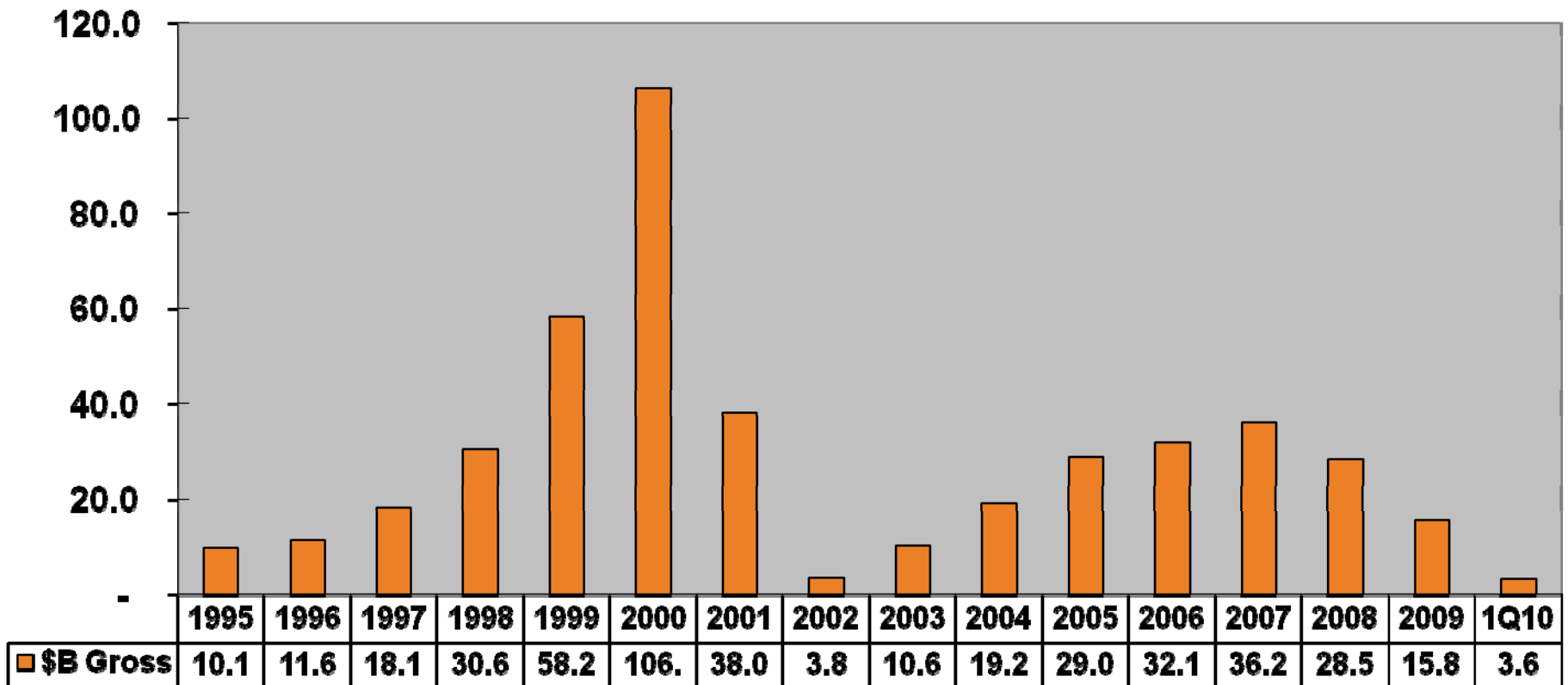


The Number of US VC Firms Has Peaked - Thankfully

<i>At Year End</i>	<i># Venture Firms</i>	<i>Capital Under Mgt</i>
1970	28	\$1B
1980	91	\$4B
1990	390	\$29B
2000	882	\$225B
2006	1022	\$277B
2009	794	\$179B

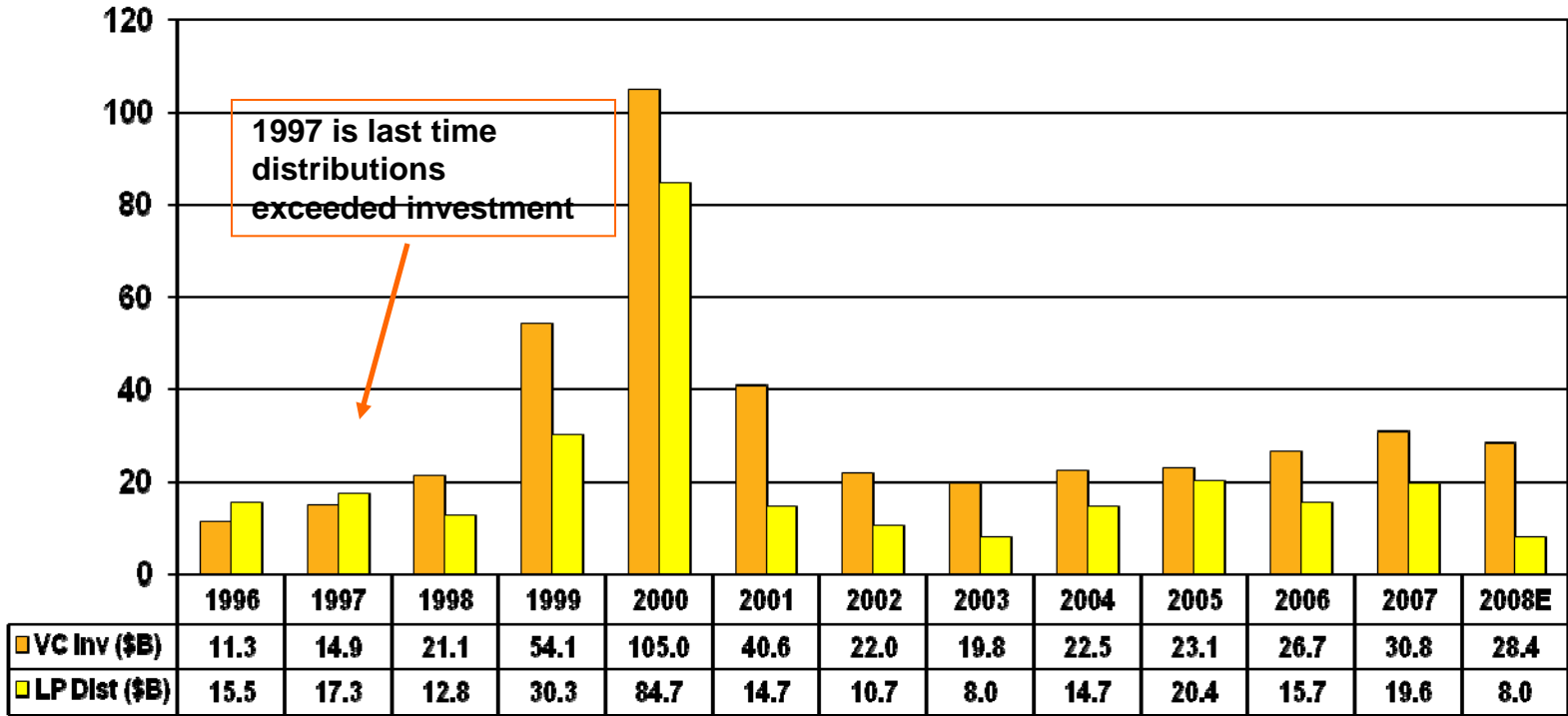
Source: 2008 NVCA Yearbook, prepared by Thomson Reuters, figure 1.04

VC Fundraising Down Considerably – A New Size Band for the Industry?



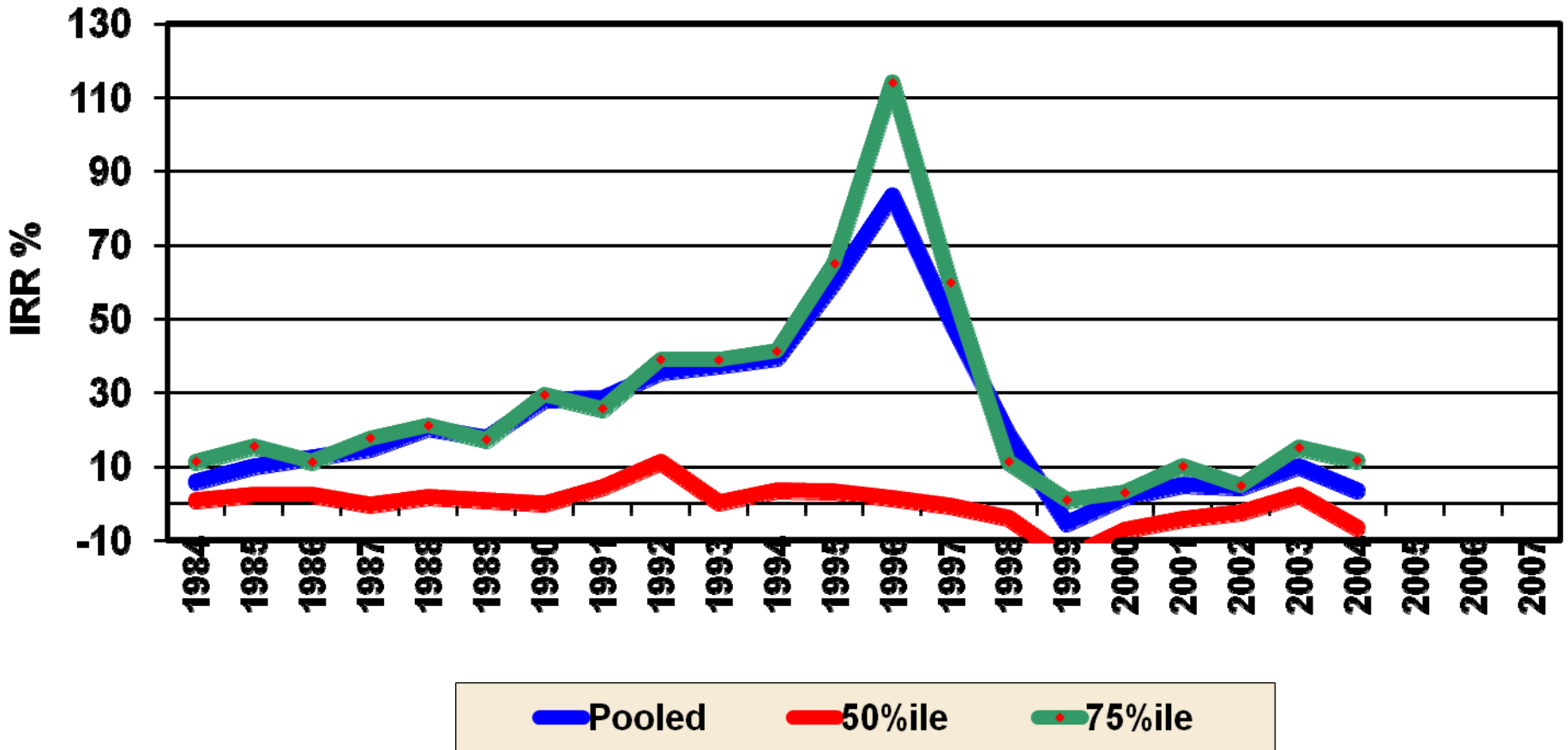
Does not include Corporate Venture groups.

Since 1997, VC Investment Exceeded Distributions; Much is Bottled Up in NAV



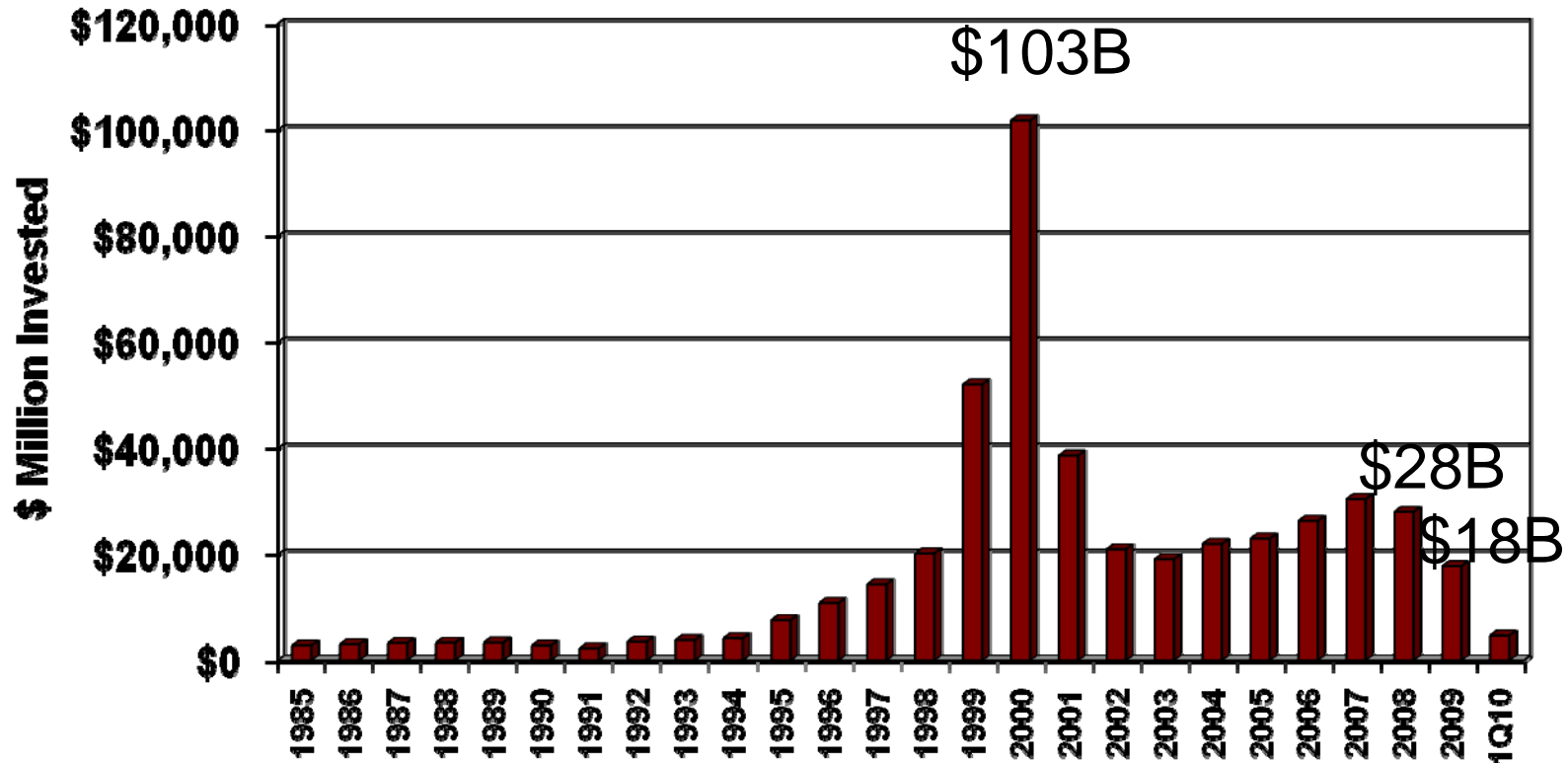
Source: Thomson Reuters/National Venture Capital Association

Industry Returns Have Been Driven by Top Quartile Funds



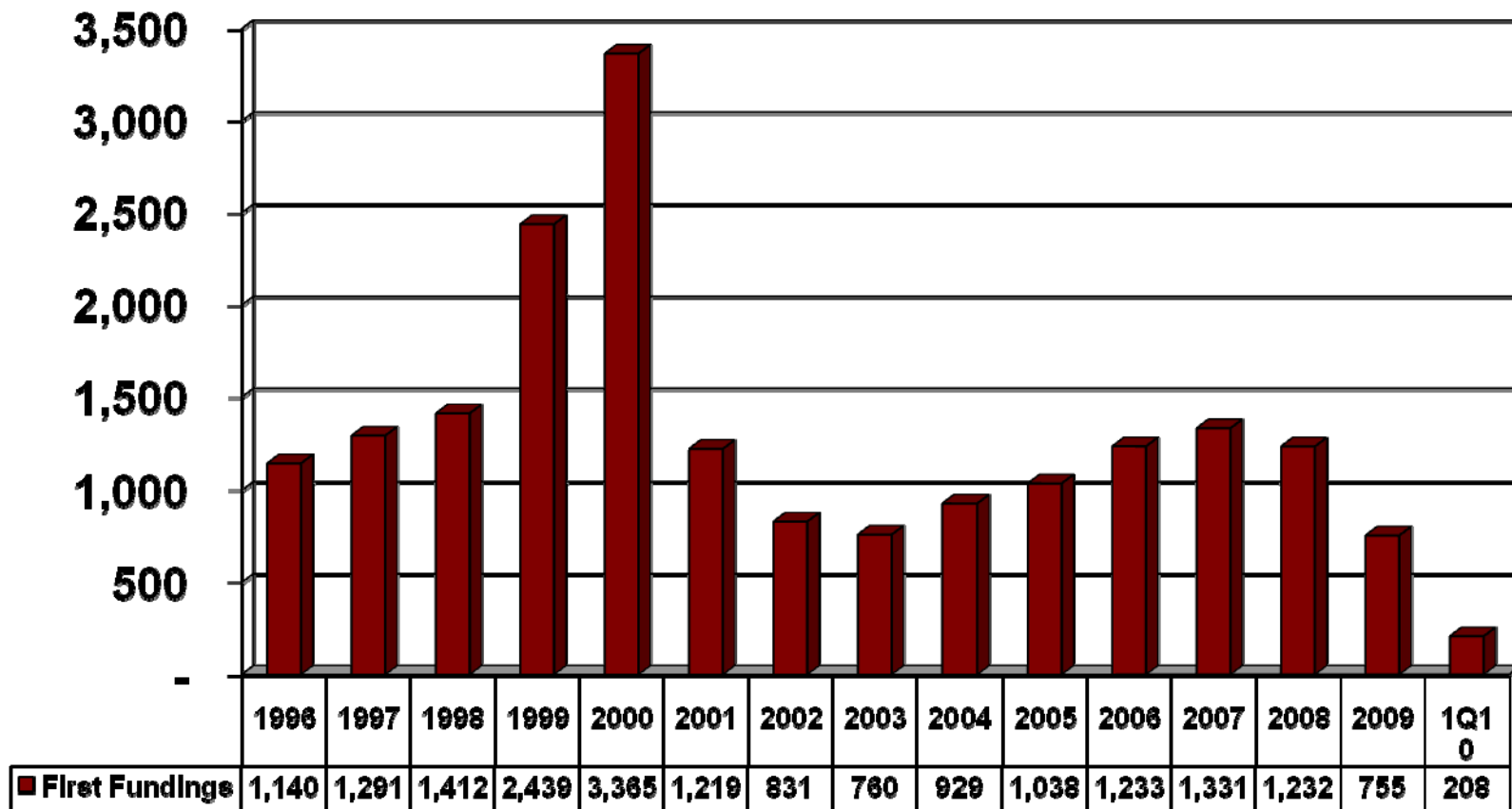
Source: NVCA 2008 Yearbook prepared by Thomson Reuters

VC Investment Peaked in 2000; 2008 Down 8%; 2009 at \$18B



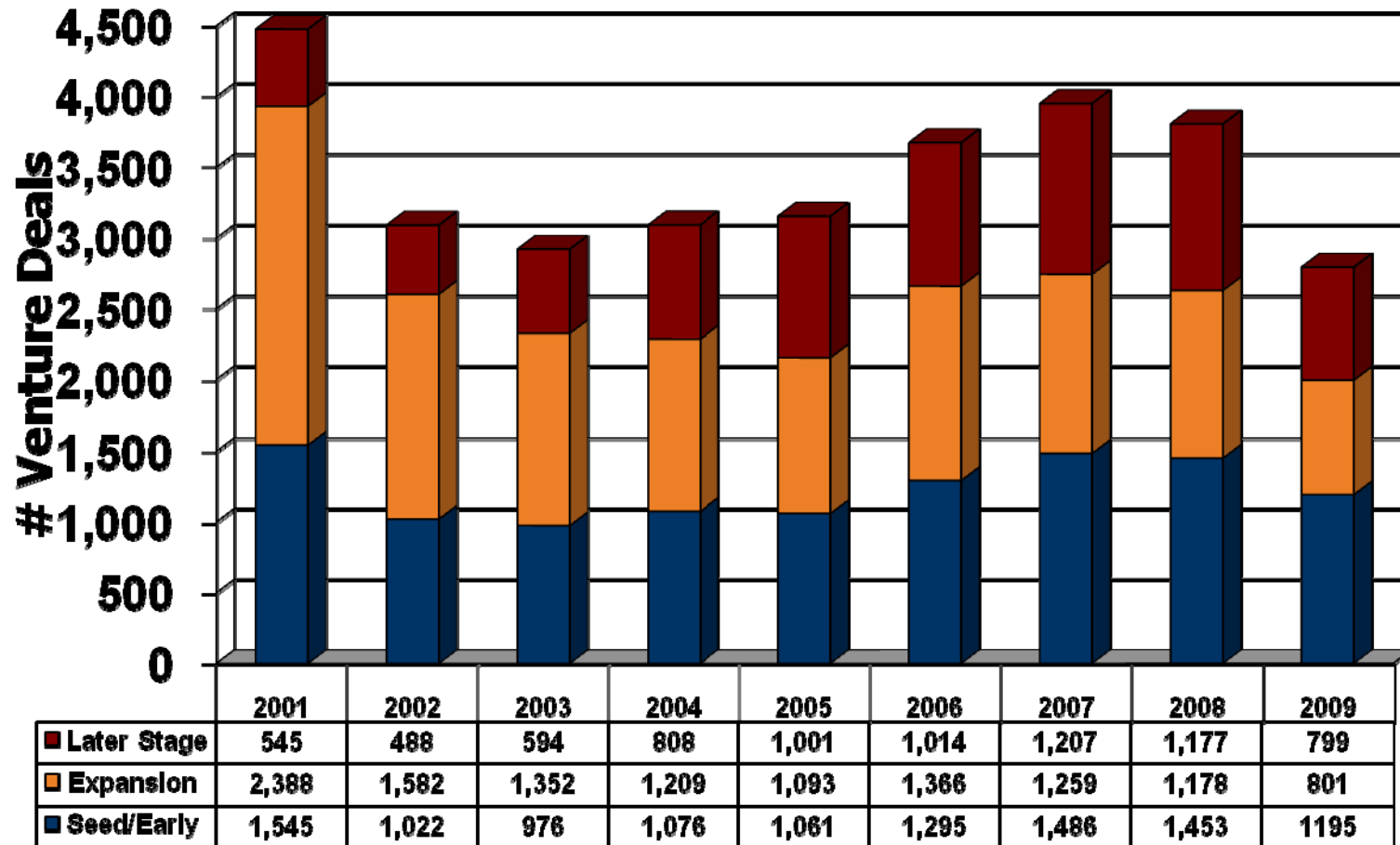
Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report,
Data: Thomson Reuters

Despite Economic Turbulence, VCs funded 1,232 new companies in 2008; 755 in 2009



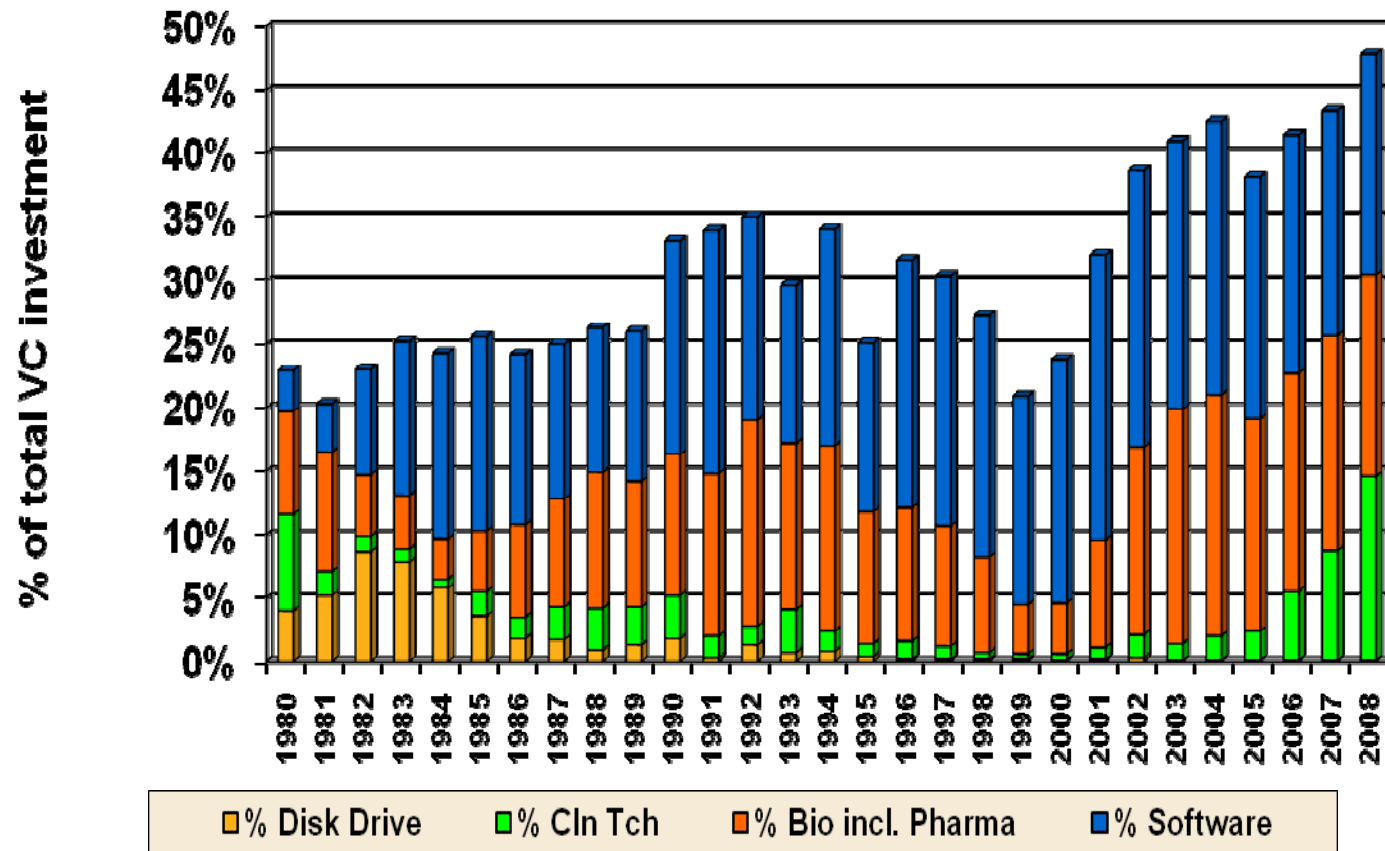
Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report,
Data: Thomson Reuters

...yet an Unprecedented Number of Companies are Receiving Later Stage Rounds



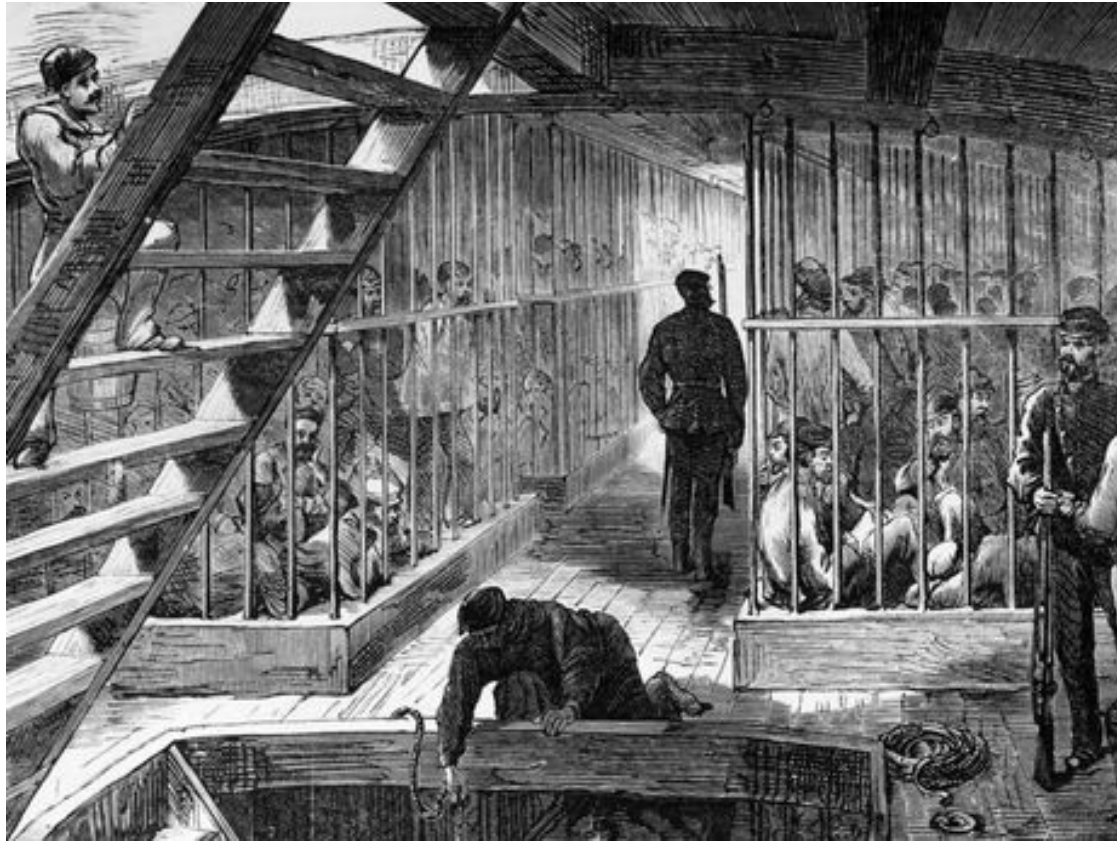
Matured But Can't Move On

“Sector Churn” - History has Shown VC Deploys Capital To Most Promising Sectors: Four Examples



Incentives & Healthcare

Pay For What You Want – The Story of How to Stop Sea Captains Killing Their Passengers



Source: Alex Tabarrok, George Mason University – “Marginal Revolution”

<http://www.npr.org/blogs/money/2010/09/09/129757852/pop-quiz-how-do-you-stop-sea-captains-from-killing-their-passengers>

Gatekeeper Incentives and Product Implementation

How healthcare gatekeepers are paid under new product paradigm affects successful adaptation – examples:

- **DUROS technology:** Developed a leuprolide 3 to 12 monthly implant (for prostate cancer treatment), vs. existing monthly formulations. Product both better and more convenient for patients, but would decrease medical provider reimbursement. Outcome: product failed in market
- **Other new oral anti-cancer formulations:** offer comparable efficacy and improved convenience vs. existing IV chemotherapy treatments, would also decrease provider visits and compensation. Outcome: products have not been adapted
- **Procedures:** Numerous examples of well-compensated procedures performed without appropriate indication (vs. effective but poorly-compensated procedures)

MHS Must Influence the Evolution of Public and Private Systems

- The MHS is not an island:
 - Not sufficient to put your own house in order - **interdependency** with the civilian health system means you have a big stake in shaping policy evolution outside the MHS for the better
- GOAL for discussion:
 - Influence public policy makers to create a health system that aligns the **interests of individuals** – consumers and providers (and industry) – with **quality and cost effective outcomes**

Examples of healthcare incentive reform

- Reduce defensive medicine through **tort reform**
- Continue to **reward innovation** (accept some degree of high prices for new breakthroughs that work for a limited period of time - ?10-14 ten years) and then rapidly promote competition and price drops
- **Remove barriers to interstate competition** in insurance and provision of healthcare
- Mandate **only catastrophic coverage**. Remove minimum coverage regulations (or accept unnecessarily higher costs and less competition and most importantly gaps in health care coverage). [Exceptions: children]
- **Encourage experimentation**. Different communities and different people within those communities will do better within different healthcare systems. **Embrace variation** as a learning opportunity, but need to **measure results, track variance** and circulate and communicate advances in knowledge and experience to accelerate learning
- **Empower individual consumers**, but ensure they have some exposure to the costs of their healthcare choices

Challenges for VC Backed Companies Pursuing Military Priorities

Venture Backed Companies Have Limited Swings At Bat to Hit a Home Run...

- ...So each swing has to count, and the consequences of missing means a good company will go down.
- Implications:
 - **Market Failure:** Strict consideration of economics and market potential selects away from targets that are important, but cannot deliver return.
 - Example: Anti-infective companies working on pathogens of high potential harm, but limited everyday commercial relevance - e.g. viruses like Ebola and Marburg and bacteria like *Acinetobacter* and *Bacillus anthracis*
 - **Regulatory Gauntlet** – New drugs and devices face high regulatory barriers to approval, and delays add significantly to the costs of development. Therefore, companies must consider how to avoid **false negative signals**.
 - Example: Euthymics

Euthymics Quick Overview

- One late phase II antidepressant asset
- One late preclinical asset for ADHD/neuropathic pain
- Additional 5+ preclinical compounds for treatment-resistant depression, anxiety, obesity, substance abuse, cognition
- Just completed \$24m series A to fund antidepressant through phase II/III trial
- Euthymics brings together scientists who successfully developed Prozac (fluoxetine), Cymbalta (duloxetine) and Strattera (atomoxetine) for depression, neuropathic pain and ADHD, respectively

Euthymics Program Overview

- EB-1010, an antidepressant in late-stage development for Major Depressive Disorder patients not responding to one course of SSRI
 - Two thirds of MDD patients do not respond to SSRIs
 - Triple reuptake inhibitor with highest potency against 5-HT, half against NE and one eighth against DA
 - This compound has among the highest treatment effects of any antidepressant in development (~ 3 x the efficacy of SSRIs)
 - Unbalanced profile allows good efficacy while preserving sexual and cognitive function without causing weight gain
- EB-1020, a NE/DA reuptake inhibitor for ADHD and neuropathic pain in late research-stage development
 - Novel efficacy profile on pain unlike other monoamine drugs
 - Works on both early (acute) as well as late phase (chronic) pain
 - Potential for good efficacy in ADHD without drug abuse liability

Euthymics Military Initiatives: EB-1010 for PTSD

- Estimated lifetime prevalence of PTSD among Vietnam veterans is 30.9 for men and 26.9 for women (from the National Vietnam Veterans Readjustment Study)
- Euthymics has consulted with one of the leading experts in the PTSD field, Dr. Jonathan Davidson, Duke University
- Triple reuptake inhibitor has the potential for improved efficacy and in particular, improve substance abuse outcomes
- **The problem:** Negative outcomes, particularly the suicide rate for veterans with PTSD is so high that Euthymics could risk the overall depression program if we initiated studies in PTSD
- **The dilemma:** PTSD is a major morbidity for our soldiers. How can Euthymics conduct studies in PTSD if these patients have poor outcomes for reasons that may have nothing whatsoever to do with EB-1010?

Euthymics Military Initiatives: EB-1020 for PLP

- About 1.2 million Americans have lost limbs and another 185,000 have amputations annually
 - *Over 1000 U.S. soldiers have had major limb and partial amputations during the Afghan and Iraq wars*
- **Phantom Limb Pain (PLP)** is distressing, debilitating and occurs in as many as 80% of amputees; 60% of patients continue to have PLP after one year
- Standard peripheral pain medications are relatively less effective, though SNRIs are effective in reducing PLP
- EB-1020, based on its activity in animal models and action of compounds with similar pharmacology, could be potentially more effective in PLP because of the DA addition to NE
 - **The Problem:** How can Euthymics gain DoD funds to access the military network to plan studies in soldiers with PLP?
 - Our current depression program with EB-1010 will entirely consume the \$24m raise

Appendix

NVF: Two Choices for Capital

■ Novartis Venture Fund

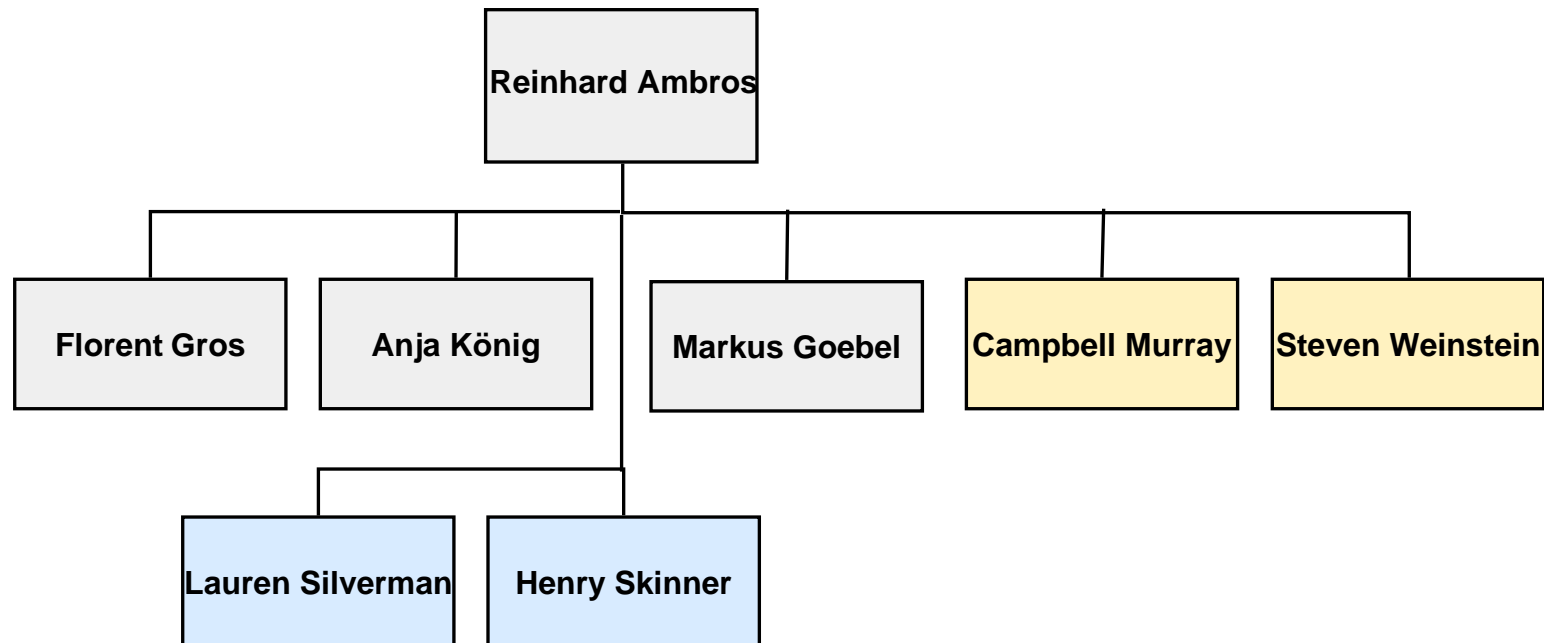
- 14 year old evergreen fund, ~\$550 mio (asset base)
- Stage neutral, bias on early stage, Series A and B for initial investment
- Biotech, medical devices, diagnostics
- Typical total commitment \$10-20 mio

■ Novartis Option Fund

- 3 years old, \$200M (asset base)
- Focus on seed and Series A for initial investment
- First investment typically \$2-6 mio plus option fee, total \$10-20 mio
- Only companies with broad technology base qualify for limited option structure

An Experienced Team with Diverse Skills

Strong combined: Pharma/Biotech R&D, BD&L, M&A, Legal, VC, Entrepreneur background



Basel

Cambridge
Venture Fund

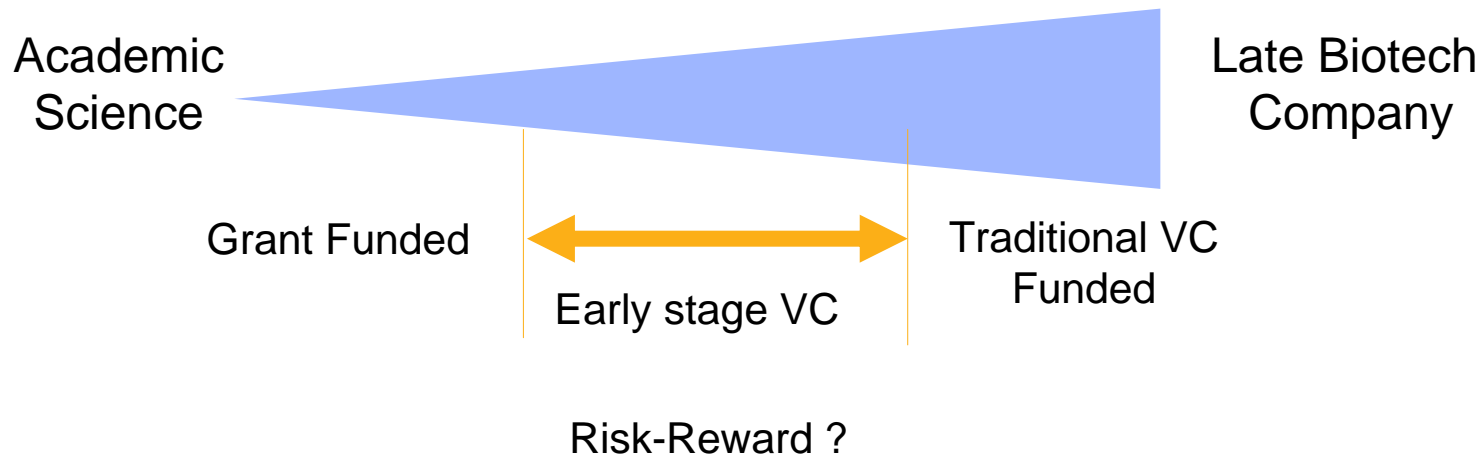
Cambridge
Option Fund

NVF Investment Process

- Screen ~1000 companies and proposals per year
- Of the screened companies <1% conclude with an investment
- Typically lead syndicate
- Multi-stage due diligence process with investment decision vested in the Novartis VC team and reviewed by independent board
- New investments +/- 25% stake, typically with board seat
- Follow on investments dependent on operational performance and financial discipline
- NVF is a long-term partner to develop the company and find profitable exits

NVF as Early Stage Investor Help to Close the Funding Gap

- The NVF team is providing strategic development support and operational expertise
- Early stage investors with longer term horizon enable risky innovations
- A combination of early stage VC and non-dilutive financing is needed to enable Bio-tech industry development



Corporate Venture Is Growing; NVF's Advantage is its Independence

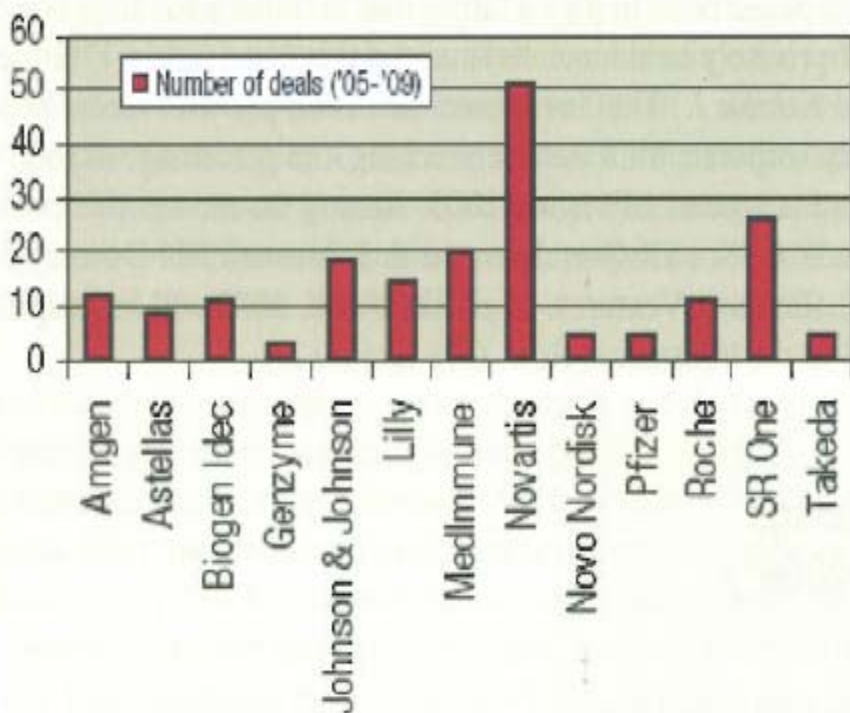
Fund	Size mio \$	People	Focus	Commitment mio \$/y	Decision driver	Geography
NVF	750	8	Bio / medt. / diag	120	Team, Adv Board	NA, EU, Korea
SROne	600	10	Bio / medt.	70	Team, CEO	NA, EU
Lilly	200	5	Bio	40	Team, BD	US
Novo	750	10	Bio	100	Team	US, EU
Roche	BS	6	Bio / diag	50	BD	US, EU
AZ	BS	4	Bio	30	BD	US
J&J	BS	8	Bio / medt. / diag	50	BUs	US, EU, Israel
Genzyme	BS	2	Bio	15	BD, CEO	US
Amgen	100	2	Bio	15	BD	US
BMS	BS	2	Bio	new	BD, M&A	US
Pfizer	BS	8+	Bio / medt. / serv.	new	BD	US, EU

**New Corporate Venture groups being started in
Healthcare (GE, Google, Merck Serono, BI ...)**

BS: Balance sheet

NVF - the Most Active Corporate VC 2005-09

Deal Activity of Selected Corporate Venture Groups (2005 – 2009)



Note: 2009 data through April 30

Source: Elsevier's *Strategic Transactions*

Lead Investor 2008/09

Company	Country
Akebia	USA
Alios	USA
Bicycle	UK
Avila	USA
Intellikine	USA
Ligocyte	USA
Merus	NL
Opsona	IRE
Oxagen	UK
Portaero	USA
Pulmatrix	USA
Sonitus	USA
Tokai	USA
Visiogen	USA

Selected Investments (2008 - 2010) where NVF was Lead Investor

Novartis Venture Fund

- Aileron (USA)
- Covagen (CH)
- ITS (UK)
- Ablation Frontiers (USA)
- Neovacs (FR)
- Akebia (USA)
- Ligocyte (USA)
- Sonitus (USA)
- Opsona (Ireland)
- Alios (USA)
- Visiogen (USA)
- Tokai (USA)
- Euthymics (USA)

Novartis Option Fund

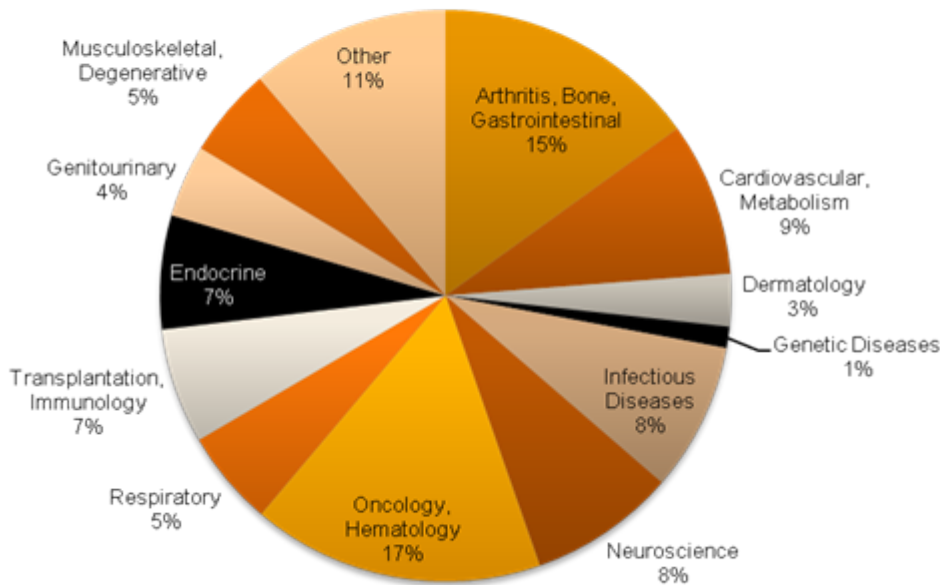
- Cequent (USA)
- Ascent (USA)
- Forma (USA)
- Proteostasis (USA)
- Heptares (UK)
- Avila (USA)

Annual investment amounts of NVF & NOF:

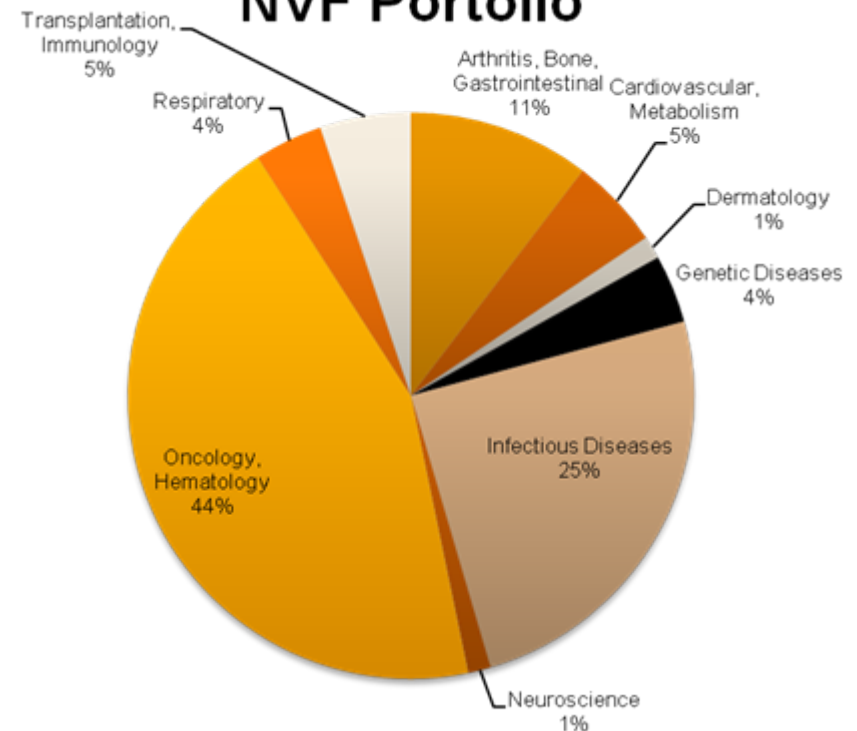
- New investments: USD~70 mio
- Follow-on investments: USD~50 mio

Industry and NVF R&D Programs by Therapeutic Area

Industry



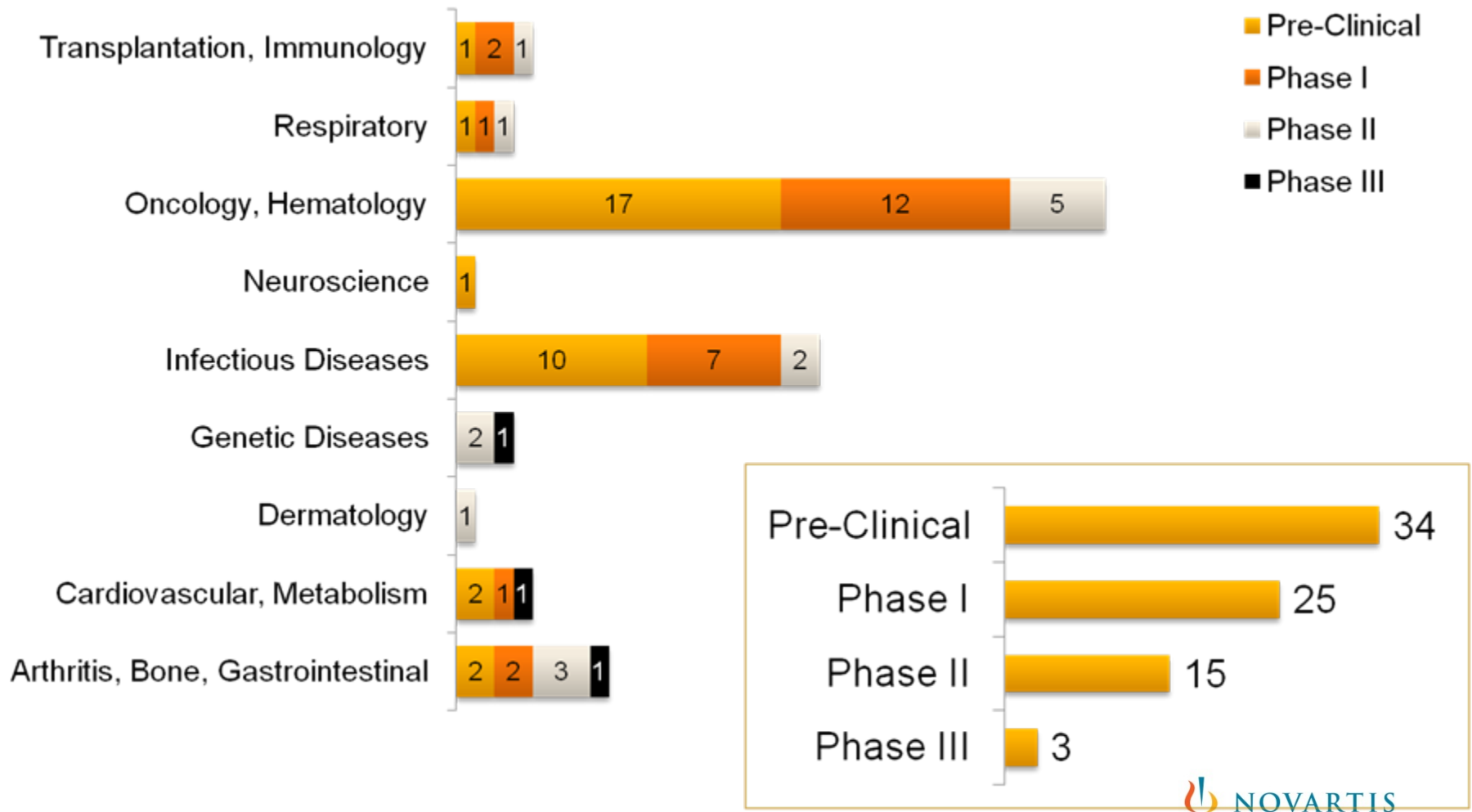
NVF Portolio



Note this table was compiled prior to the NVF investment in Euthymics which has increased Neuroscience assets under management

NVF Portfolio Companies Develop more than 70 Attractive Programs

Programs by TA and Development Stage



Exits: We Invest in Companies Others Find Attractive and Provide Substantial Returns

Acquisitions – total 21

- FoldRx -- Pfizer
- EsbaTech -- Alcon
- Visiogen -- Abbott
- Ablation Fr. -- Medtronic
- Swiss Ph. C. -- Covance
- Theravance -- GSK
- Idenix -- Novartis
- Syrrx -- Takeda
- KuDOS -- AstraZeneca
- Glycart -- Roche
- Kinetix -- Amgen
- Transform -- J&J

IPOs – total >20

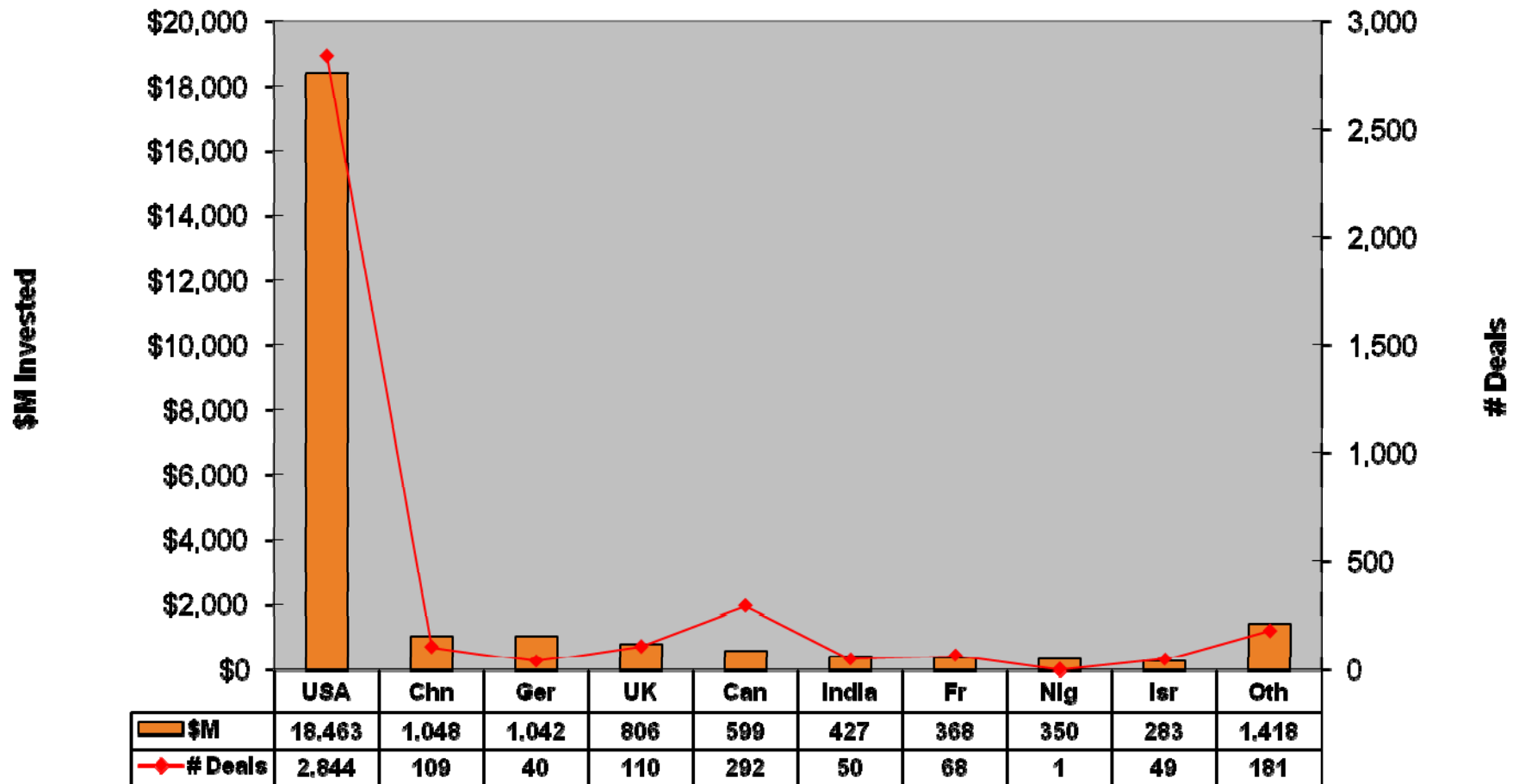
- Evolva -- holding
- NeoVacs -- holding
- Xenoport -- exit
- Eyetech -- exit
- Speedel -- exit
- Cytos -- partial exit
- Idenix -- exit
- Santhera -- holding
- Sirtris -- exit
- CombinatoRx -- holding
- Acorda -- exit

What We Stand For

- Trusted partner
- Successful investor
- Unique access to Novartis
 - Act as bridge between Novartis and portfolio
 - Access to domain expertise supports Funds to make informed decisions
 - Maintenance of confidentiality is paramount
- Integral member of the greater syndicate
 - Proactive Board member
 - Patient investor during ups and downs
 - History of supportive follow-on investments
- Transparency of motive and process

International Investments by US - Based Funds

Where US - Domiciled Venture Funds Invested in 2009



Source: ThomsonONE™ Database by Thomson Financial