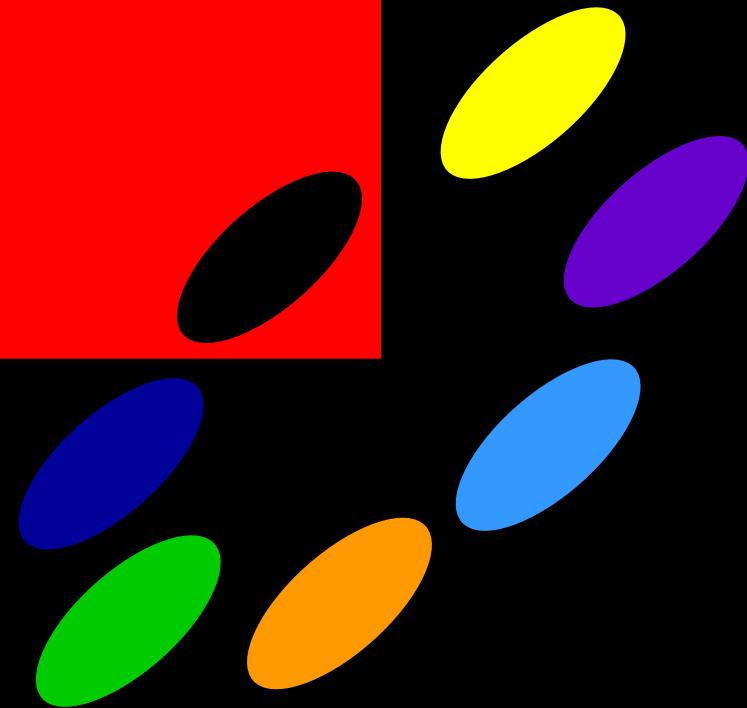


Heart of the Matter: Key Issues and Opportunities in the Cardiovascular Drug Space

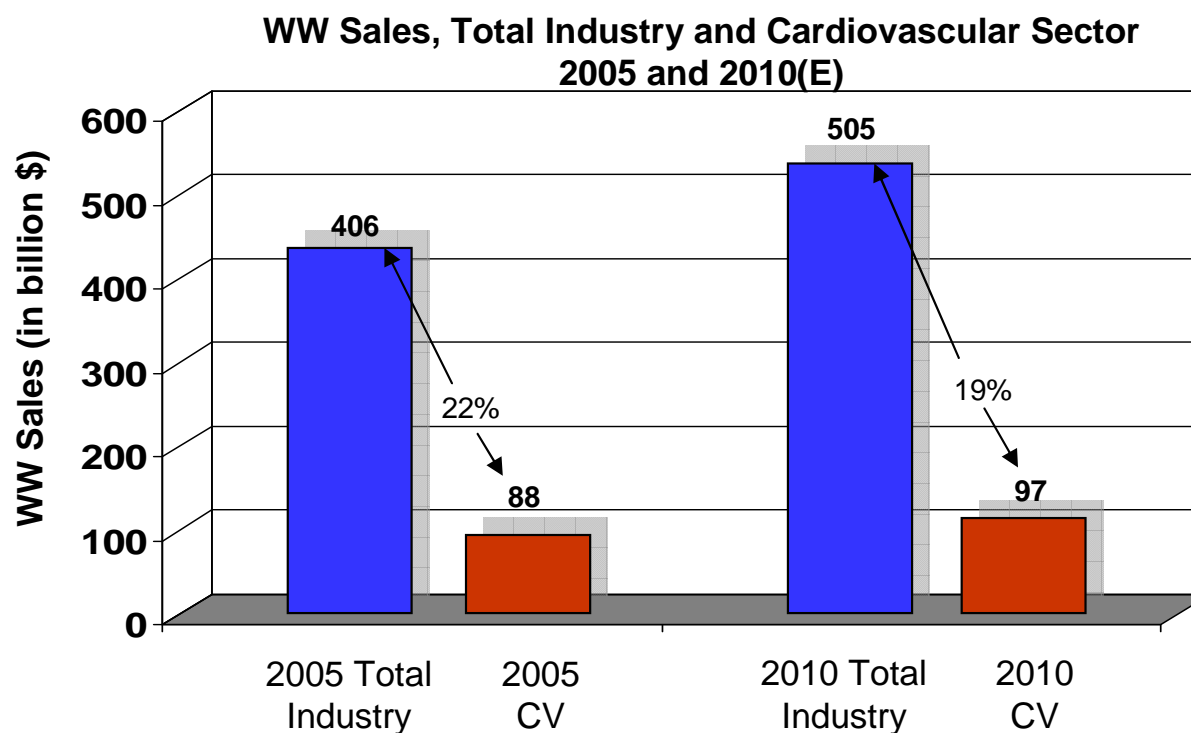
Edward C. Saltzman
President, Defined Health

Windhover's TA CardioAlliance Meeting
November 16, 2006, Chicago



CVD's Tremendous Revenue Contribution

- The cardiovascular sector has been, and will continue to be a critical component of the entire pharmaceutical industry

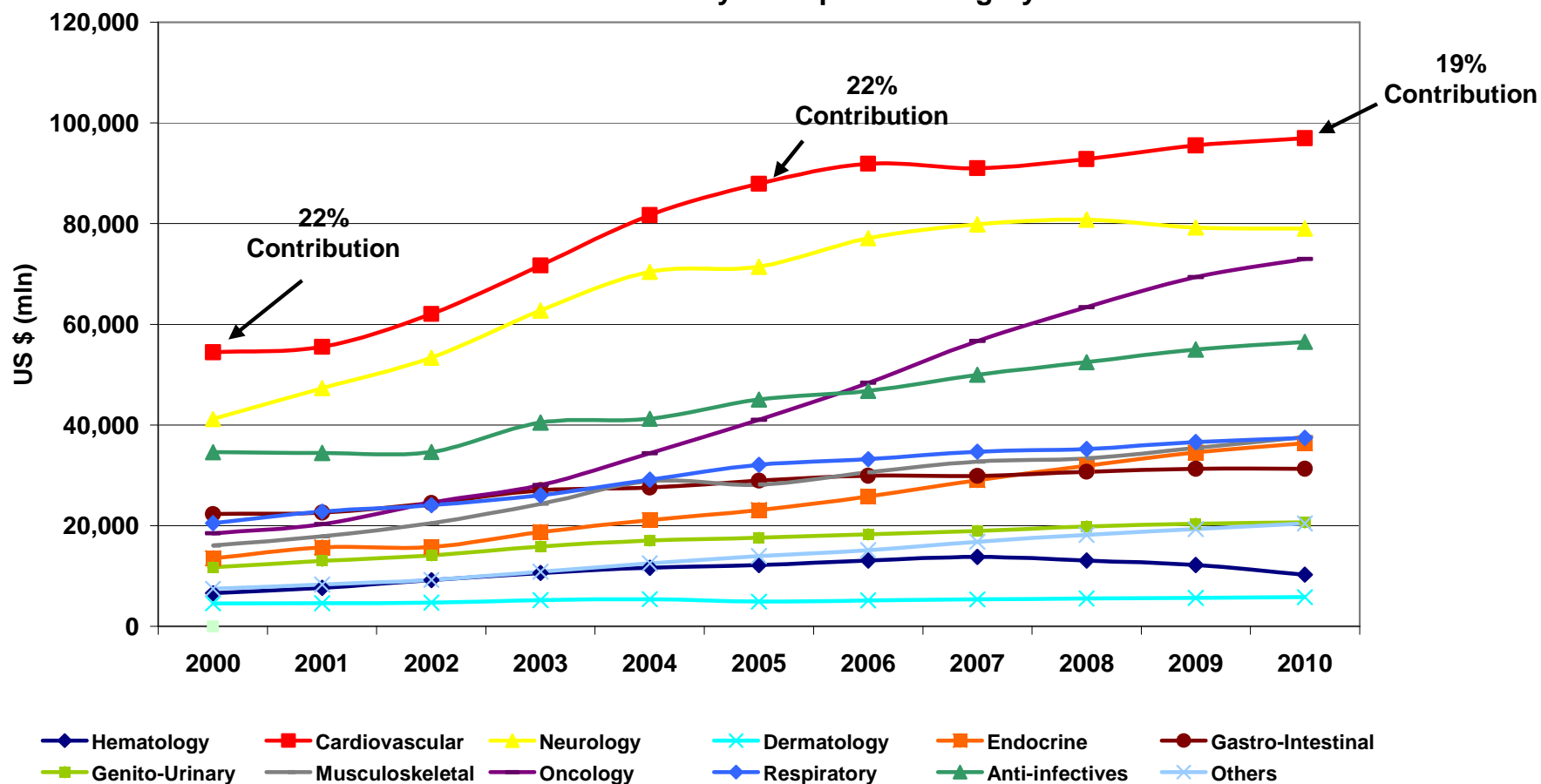


EvaluatePharma; DH Analysis

However, CVD is Declining in Revenue

- CVD is a shrinking market among the therapeutic areas in terms of share of contribution to the overall pharmaceutical market.
 - Decline is largely driven by generic erosion of off-patent products
 - Genericismation will greatly accelerate in 2011 when *Lipitor* (Pfizer) and *Plavix* (BMS, s-a) go off patent.

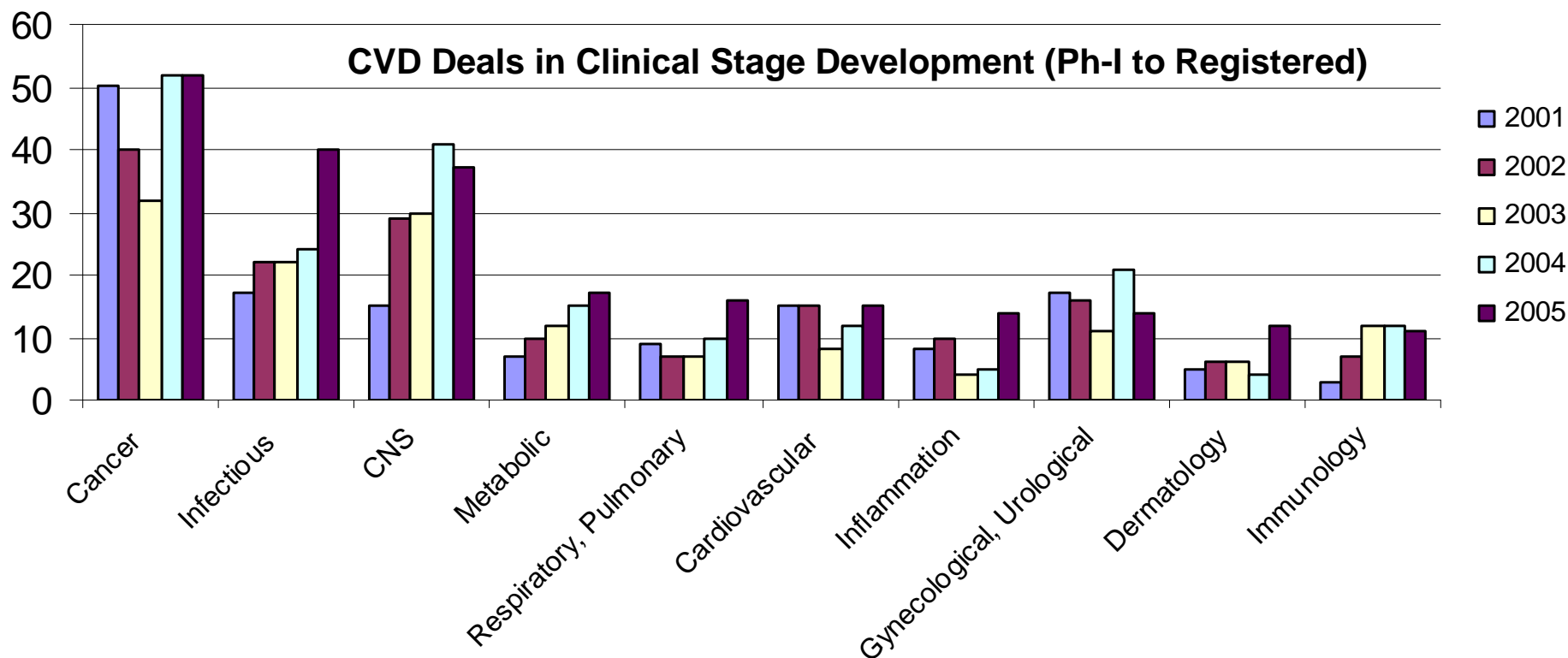
Forecasted Revenue by Therapeutic Category



Evaluate Pharma, DH Analysis

CVD Dealmaking: Opportunity or Liability?

- Few deals, despite opportunity and need to replace products losing patent protection.
 - The cardiovascular market is maturing, and much-needed commercial replacements must emerge soon for the sector to sustain its recent growth.
 - The anemic rate of transactions since 2000 indicates that available projects may be declining or potential partners are passing over opportunities.
 - Is risk intolerance forcing Pharma to shift resources away from CVD?



Windhover's Strategic Transactions Database

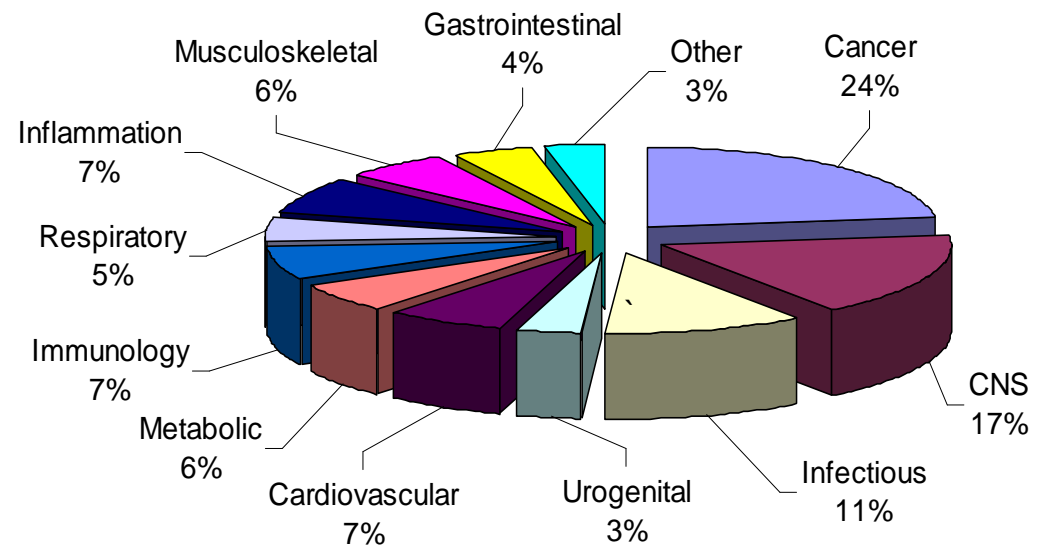
Deal Making Relative to WW Market Size

- With only 14 deals so far this year, CVD is one of the least active therapeutic areas for partnering in comparison to its size.

Number of Alliances
by Therapeutic Category
(2006 Year to Date)

Therapeutic Category	# of Deals
Cancer	47
CNS	35
Infectious Disease	23
Inflammation	15
Cardiovascular	14
Immunology	14
Ophthalmic	13
Metabolic Disorders	12
Musculoskeletal	12
Blood/Coagulation	10
Respiratory/Pulmonary	10

Proportion of 2006 Deals
by Therapeutic Category

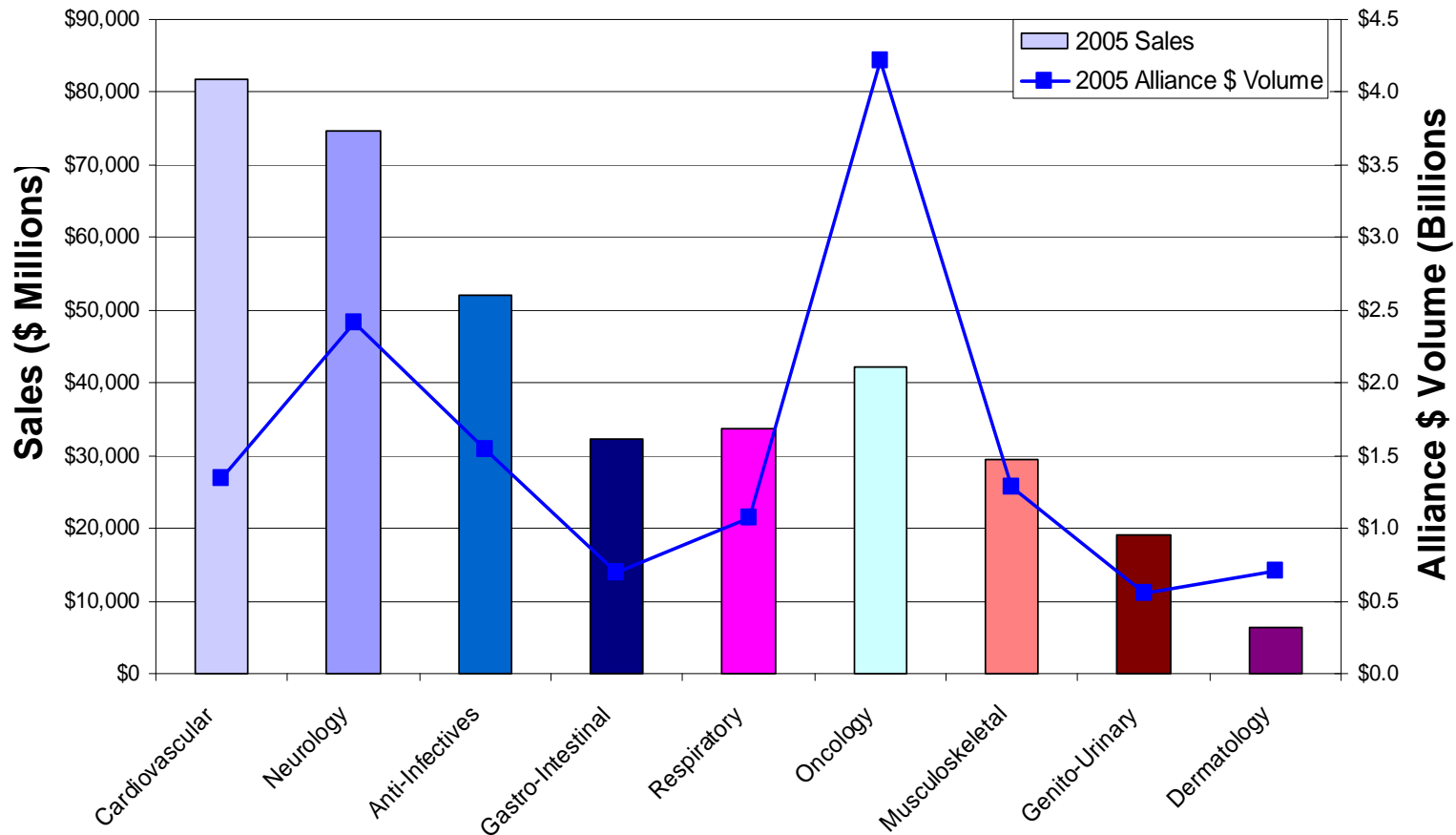


Windhover's Strategic Transactions Database

Deal Making Relative to WW Market Size

- Although CVD is the largest global market of the therapeutic areas listed below, it has attracted the least number of deals and alliance dollars in comparison to its size.

WW Sales vs Alliance Dollars (2005)



Windhover's Strategic Transactions Database, Evaluate Pharma

Why the Paucity of CVD Dealmaking?

- Top reasons DH has heard from the industry:
 1. Low unmet need / High SOC
 2. Low growth
 3. Expensive and risky development
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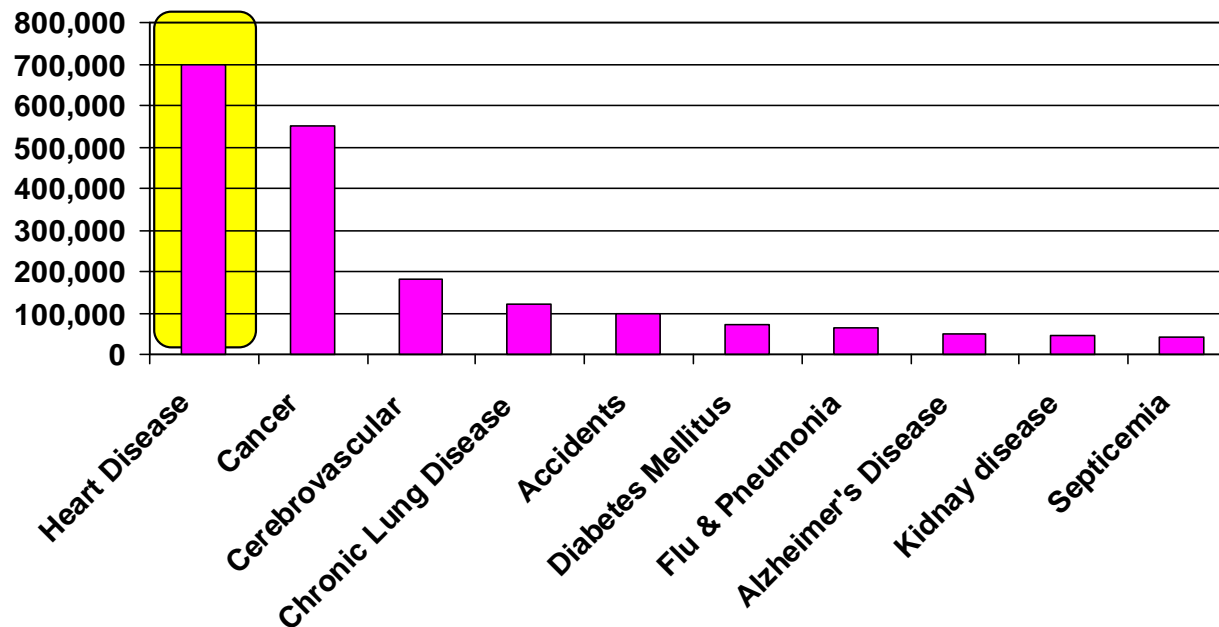
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Low Unmet Need?

- Cardiovascular Disease is the most prevalent of all diseases:
 - AHA estimates over 70M Americans have a cardiovascular condition.
 - Cardiovascular disease is the major cause of death in the US.
 - In the US alone, CVD results in nearly 700,000 deaths each year.

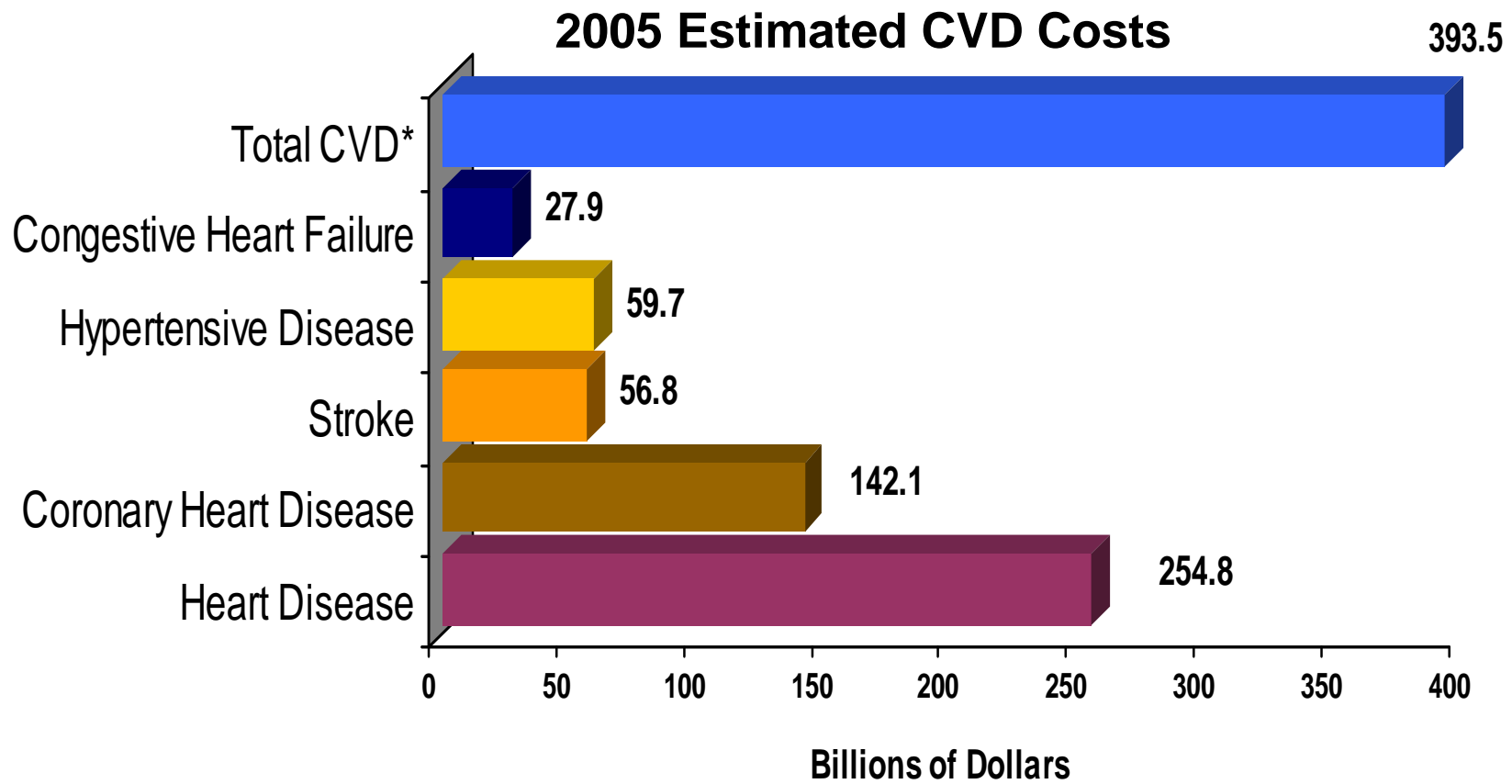
Causes of Deaths in US Annually (estimated 2006)



National Center for Health Statistics

Estimated Direct and Indirect Costs of Cardiovascular Diseases and Stroke

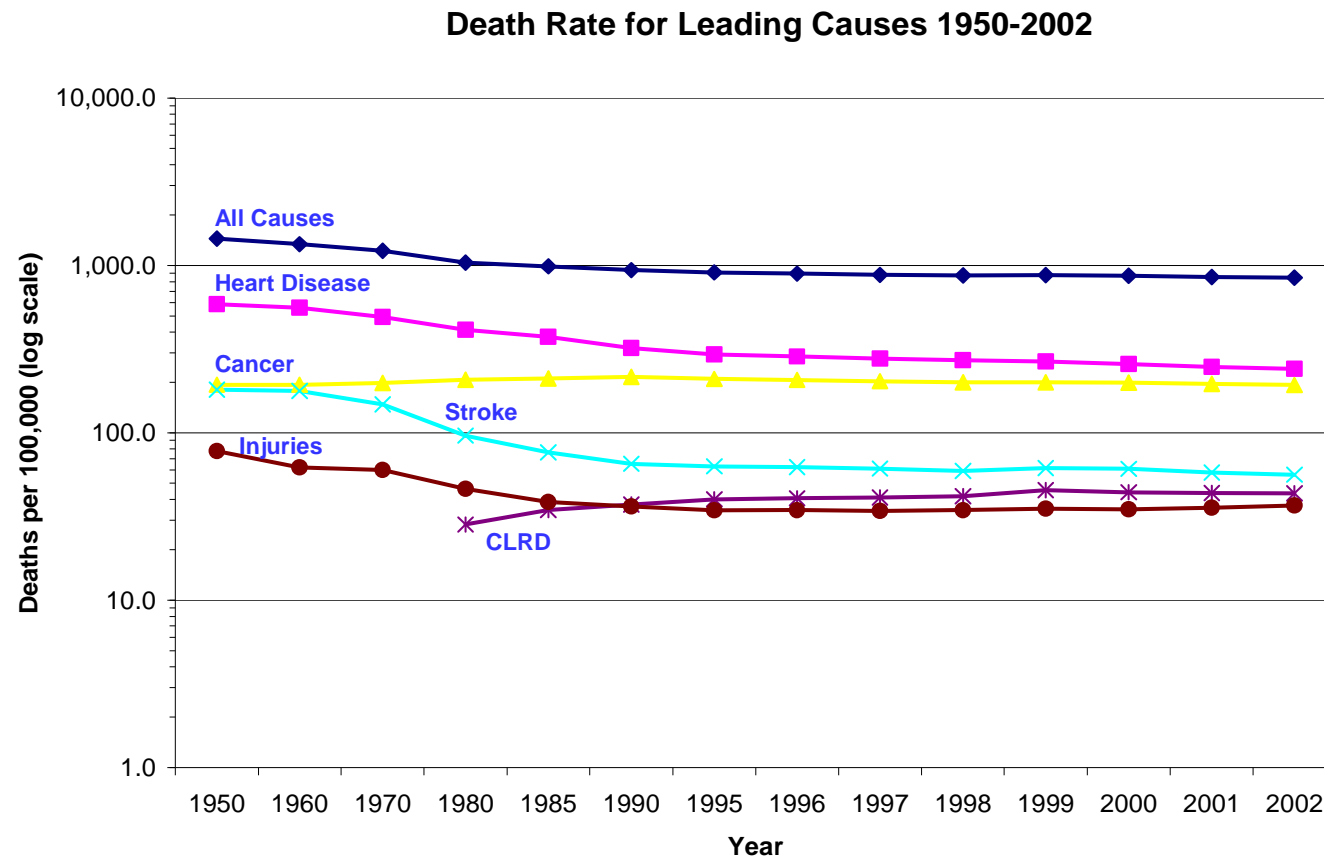
- Costs associated with CVD are estimated at over \$400 bn
- In 2006, heart disease alone is projected to cost more than \$258 billion, including health care services, medications, and lost productivity.



AHA Heart Disease and Stroke Statistics – 2005 Update.

High Standard of Care?

- In 2002, nearly 700 thousand people died of heart disease (51% of them women). This was 29% of all US deaths.
 - Despite increased chance of survival of acute events, heart disease is still the leading cause of death for both women and men in the United States



- In fact, increased survival of acute events like myocardial infarction has increased the prevalence of chronic conditions such as congestive heart failure.

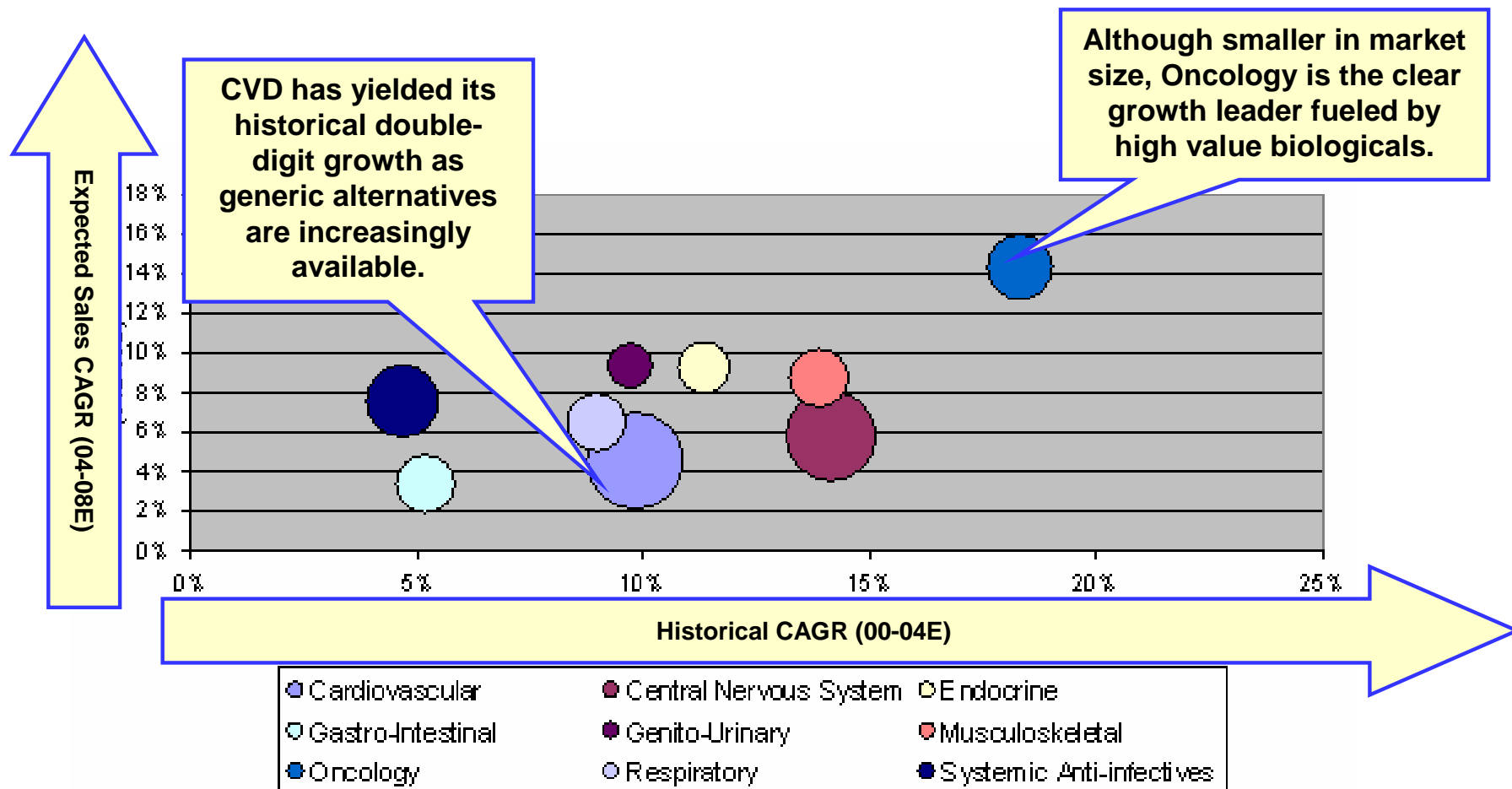
Health, United States 2005 www.CDC.gov

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Lack of Growth?

- Comparison of Past and Expected Future Growth by Therapeutic Area

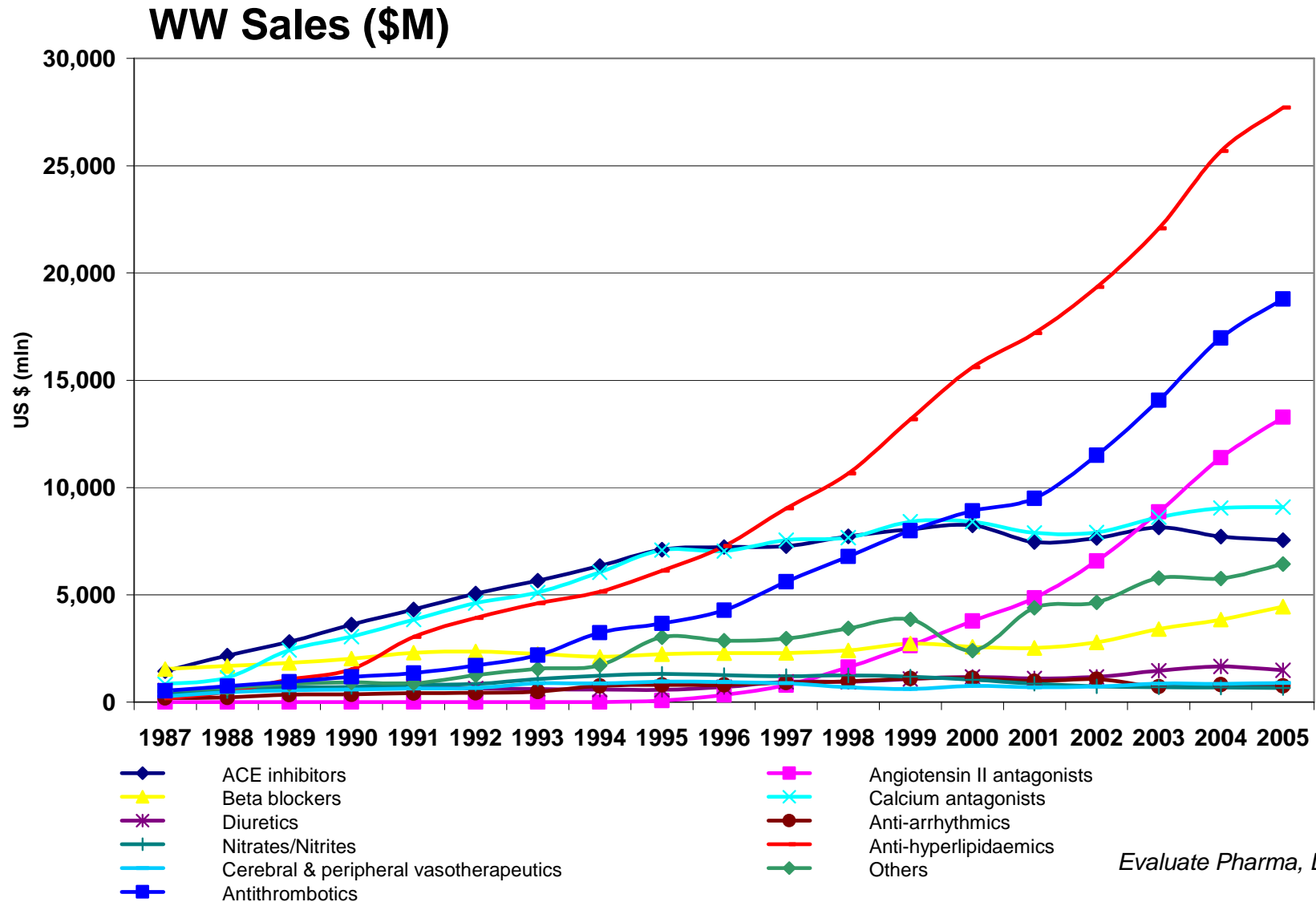


- Growth is anemic, but is this something that innovation cannot help alleviate?
 - New drugs for underdeveloped indications
 - New drug classes as additions to SOC

Evaluate Pharma, DH Analysis

Total Worldwide CV Therapeutic Category Sales, 1987 - 2005

- Statins, ARBs and Antithrombotics are leading growth.



Evaluate Pharma, DH Analysis

Lack of Growth? CVD Market in Flux

- Despite substantial increases in NRx across many categories, new prescriptions are increasingly for generic alternatives.
- Thrombosis is the only major area expected to show significant sales growth through 2010.

The market for many CVD highest value drugs is being eroded by generic competition.

COMPONENTS OF THE CARDIOVASCULAR MARKET

Drug Class	Therapeutic Target	Sales (\$MM)		\$	NRx
		2005	2010P	'05-10 CGR	'87-05 CGR
ACE Inhibitors	Hypertension, CHF	\$6,211	\$4,584	-6%	14%
Alpha Blockers	Hypertension	737	396	-12%	8%
Angiotensin Receptor Blockers	Hypertension, CHF	10,376	13,431	5%	NM
Anti-Arrhythmics	Arrhythmia	449	1,201	22%	-2%
Anti-Thrombotics	Thrombosis, Stroke	9,599	18,353	14%	NM
Beta Blockers	Hypertension, CHF	3,557	2,646	-6%	4%
Calcium Channel Blockers	Hypertension, Angina	5,967	1,650	-23%	9%
Cholesterol	Lipid Disorders	26,158	27,986	1%	24%
Diuretics	Hypertension	75	5	-42%	2%
GP IIb/IIIa Inhibitors	Thrombosis	912	722	-5%	NM
Inotropic Agents	Arrhythmia	52	15	-22%	0%
Vasodilators	Hypertension	137	200	8%	-4%
Vasopeptidase Inhibitors	Hypertension	275	363	NM	NM
Other CVD Agents	Various CVDs	4,699	6,974	8%	9%
TOTAL		\$69,174	\$78,525	3%	6%

Therapeutic Category Outlook, Cowen, October 2006

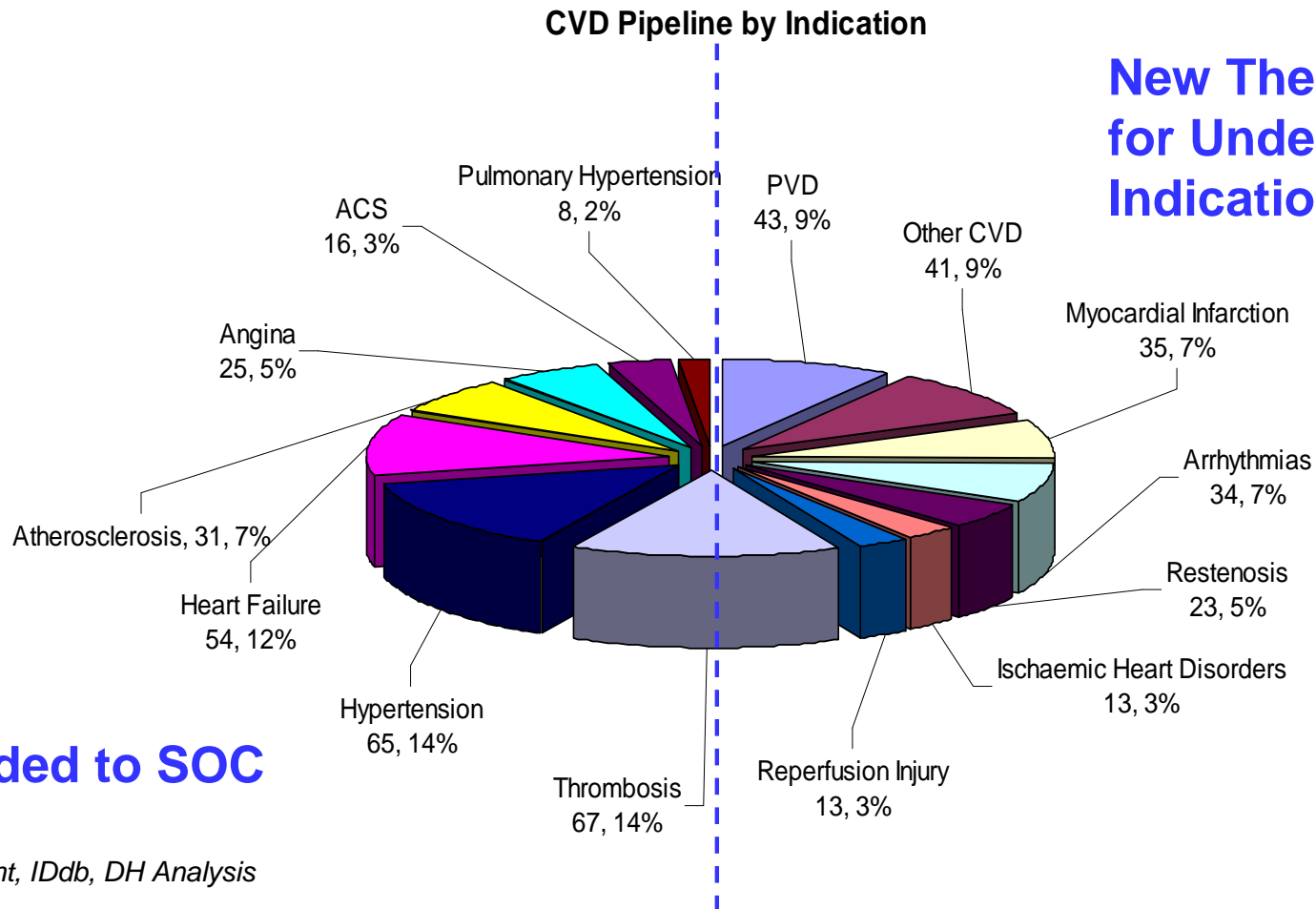
NA- Not available
 NM - Not meaningful

Source: Company data; Cowen and Company estimates; IMS America

But Slow Growth Prognosis May be Tempered by New Products for Currently Unmet Needs or Additions to SOC

Added to SOC

New Therapies for Underserved Indications



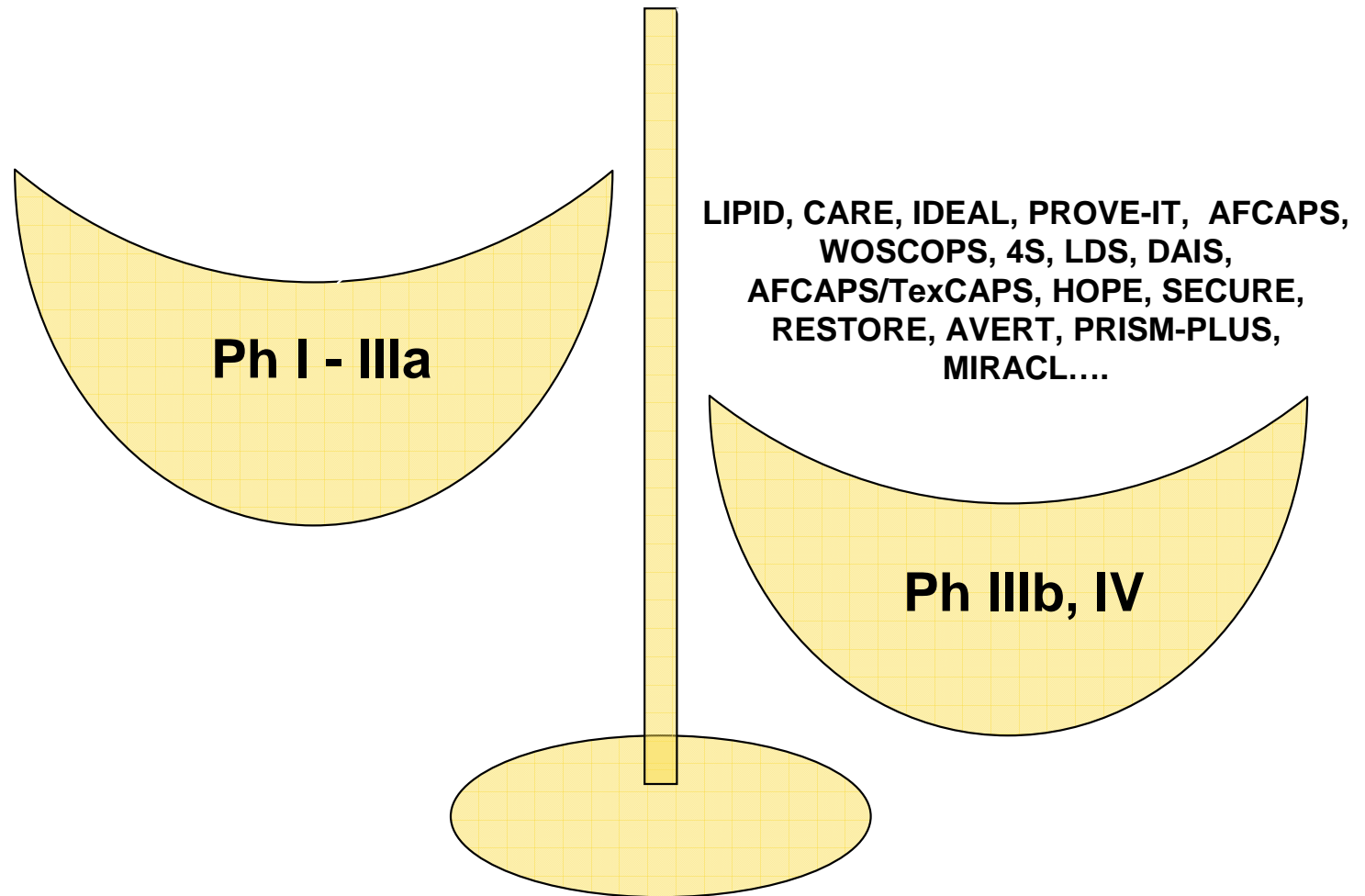
Adis R&D Insight, IDdb, DH Analysis

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Expense and Developmental Risk?

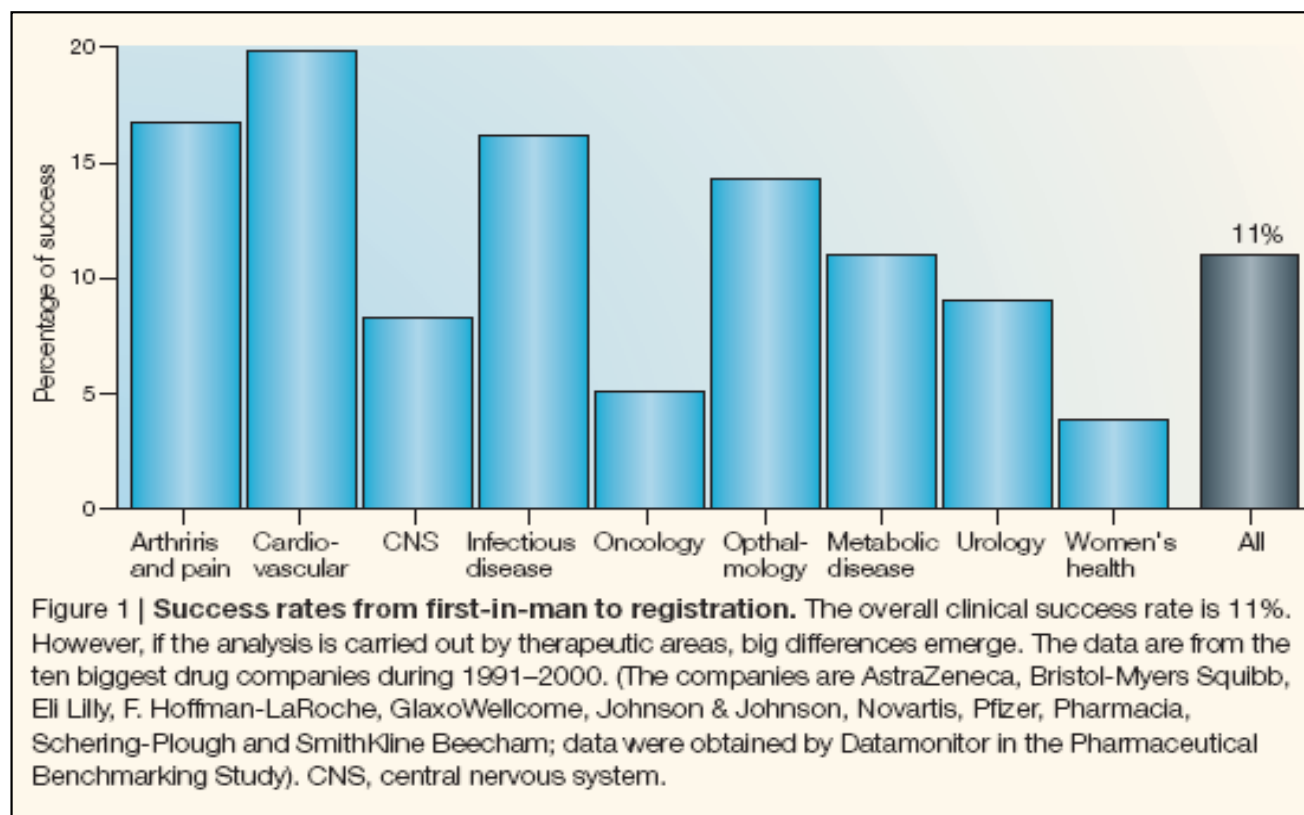
- Prevention Results are a Must
- Large Patient Numbers and Long Duration
- Near Launch Results Necessary



DH Analysis

Historically, CVD has compared favorably to other TAs in Terms of Development Risk

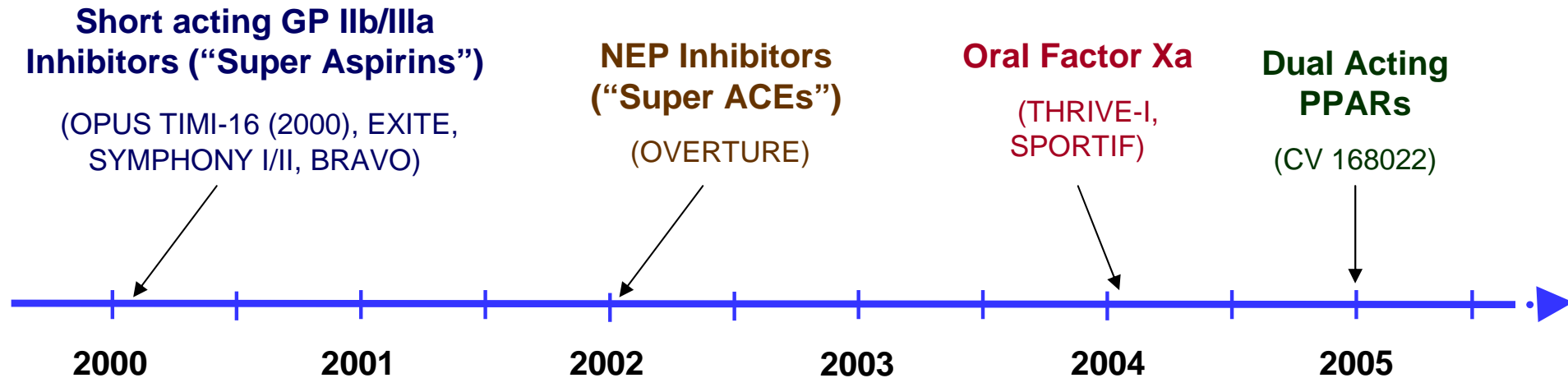
- CVD is among the most successful categories in terms of attrition rates.
- This may be skewed by the numerous “fast followers” developed in most of the major CVD drug classes once a given MOA is validated.



Nature Reviews Drug Discovery, Volume 3, August 2004, 711

TA Cardiovascular, November, 2006 - Pg. 19

However, Numerous Recent Late Stage Blow-ups Have Led Many Companies to Reconsider CVD Development Risk.



- Expensive late stage CVD trial failures have been far too frequent.
- The rising efficacy bar and safety hurdle has decreased the predictability of Phase III success based on Phase II success.
- Outcomes data has become a prerequisite for FDA approval.

DH Analysis, Company news releases, Clinicaltrials.gov

Expense and Developmental Risk?

Torcetrapib/atorvastatin (Pfizer)

- *Torcetrapib/atorvastatin, for heart disease.*
 - *This one-pill combination therapy is designed to reduce the risk of atherosclerosis by raising the levels of “good” HDL cholesterol and, simultaneously, lowering the levels of “bad” LDL cholesterol. The development work and clinical studies for this medicine will exceed \$800 million.*

THE NEXT WAVE
In 2006 and 2007, we plan to file Pfizer's next wave of new medicines with the FDA. These therapies are all aimed at serious conditions that impose hardship on patients and their caregivers, and considerable expense on healthcare systems everywhere. These new medicines are:

- Maraviroc, for HIV/AIDS. Maraviroc selectively binds with the receptor that HIV uses to enter uninfected cells.
- Avenavine, for schizophrenia and bipolar disorders. Versatile, easy-to-administer and well-tolerated, avenavine would add to the options physicians already have in Geodon, to treat these recurrent and complex conditions. Avenavine is being developed in partnership with the Organon unit of Alzo Nobel.
- Tislelizumab, for cancer. This CTLA-4 monoclonal antibody will fight life-threatening cancers by helping a person's immune system recognize and selectively destroy cancerous cells. Tislelizumab is being developed by Pfizer in collaboration with Abgenix.
- Torcetrapib/atorvastatin, for heart disease. This one-pill combination therapy is designed to reduce the risk of atherosclerosis by raising the levels of "good" HDL cholesterol and, simultaneously, lowering the levels of "bad" LDL cholesterol. The development work and clinical studies for this medicine will exceed \$800 million.

NEW STANDARDS OF PRODUCTIVITY
While we have achieved new heights in R&D productivity, our R&D processes must be made even more robust to sustain our growth well into the next decade. Today we are implementing new organizational structures that both streamline our R&D processes and refocus them on advancing the science. For example, by adapting new approaches to information technology, we have created far more efficient IT service models. The result: more resources can be redeployed into biomedical discovery and development. We have also created a number of "global centers of excellence" in functions such as pilot plant production and high throughput compound screening. For example, global biologics development and manufacturing is now consolidated into a single R&D site in St. Louis, Missouri. Again, the results lead to more funds available for investment in the projects that lead directly to new medicines.

JOHN AND LINDA DWYER
"More time with her family was the only thing that mattered to her."

Linda Dwyer's daughter Kelly speaks of her mother today in the present tense because, "even though she's not here with us physically any more, she lives on in so many people." Linda, who was featured on the cover of Pfizer's 2005 Annual Review, died in 2005.

Her legacy lives on not only in her three children, Inge, Kelly and Brandon, but also in the countless people she helped by her participation in the Phase III clinical trials for S-11,245, developed by Pfizer's La Jolla labs and now available to patients as Satazet. Without clinical trials and the extraordinary bravery of patients like Linda Dwyer, new life-saving medicines would not exist. "I will never see bravery and courage like Linda's," her husband John says, referring to the nine major surgeries and the 300-plus medical procedures she endured through her seven-year battle. "Seven years of love, happiness, growing and memories. Without all that extra time, my brothers and I wouldn't have had the chance to know my mom like we know her today," Kelly says. Whether Linda was enjoying a birthday visit to the David Letterman show, watching her son's hockey tournament at Lake Placid, enjoying the annual summer vacation at Orchard Beach, Maine, or seeing the Boston Red Sox win the World Series, she knew, John says, that the "only thing that matters in life is life itself."

2005 Pfizer Annual report

Torcetrapib/atorvastatin (Pfizer)

Pfizer Drug Dealt Blow in Testing

The New York Times
nytimes.com

By [ALEX BERENSON](#) November 1, 2006

[Pfizer](#) said yesterday that clinical trials of torcetrapib — a heart medication that is the most important drug in the company's pipeline — confirmed that it raises [blood pressure](#), a potentially serious side effect.

Any problems with torcetrapib would be a serious setback for Pfizer, the world's largest drug company. Pfizer has been counting on the new medicine to eventually replace the \$13 billion in annual sales from the [cholesterol](#)-lowering drug Lipitor, which loses patent protection in 2010.

Cardiologists and Wall Street analysts alike have been closely watching the clinical trials of torcetrapib, a medicine intended to raise so-called good cholesterol.

Pfizer's stock dropped 2 percent after the announcement by the company, which has been researching torcetrapib for a decade and is spending \$800 million to develop it.

Pfizer said it still expected to submit the medicine for federal approval sometime in the second half of next year, with an approval possible in 2008. Pfizer hopes to win approval by showing that a combination of torcetrapib and Lipitor can reduce the formation of plaque in the arteries.

But doctors said that the blood pressure rise was medically significant and would discourage the [Food and Drug Administration](#) from approving torcetrapib, even if Pfizer proves next year that the drug does reduce plaque. Instead, Pfizer will now probably have to show that torcetrapib actually lowers the risk of heart attacks and strokes in patients who take it, not just that it cuts plaque, the doctors said.

Pfizer is conducting a 25,000-patient trial to examine whether torcetrapib reduces deaths and heart attacks. But full data from that trial will probably not be available until 2009. The findings described yesterday were preliminary results from more than 4,000 patients already enrolled in that trial.

Among those patients, Pfizer said, torcetrapib caused an average rise of three to four millimeters in their systolic blood pressure, the top number of the blood pressure reading. In other words, a person who had a blood pressure reading of 125 over 80 before entering the trial would generally have a reading of 128 over 80 or 129 over 80 after taking the drug. The difference may seem small, but cardiologists said it was troubling.

"It is a concern," said Dr. Antonio M. Gotto Jr., a cardiologist and the dean of Weill Cornell Medical College in New York. "It doesn't mean the death knell for the drug, but it would probably mean that one would want to see evidence on clinical events before approving the drug."

Earlier clinical trials had also shown that torcetrapib raised blood pressure, but analysts and some doctors had hoped that the effect would decrease in the larger trials. Instead, patients in the new trials actually had an even larger gain in pressure.

Why the Paucity of CVD Dealmaking?

- Top reasons DH has heard from the industry:
 1. Low unmet need / High SOC
 2. Low growth
 3. Expensive and risky development
 - 4. Huge promotional expense**
 5. Big Pharma internal pipelines are adequate
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Enormous Promotional Expense

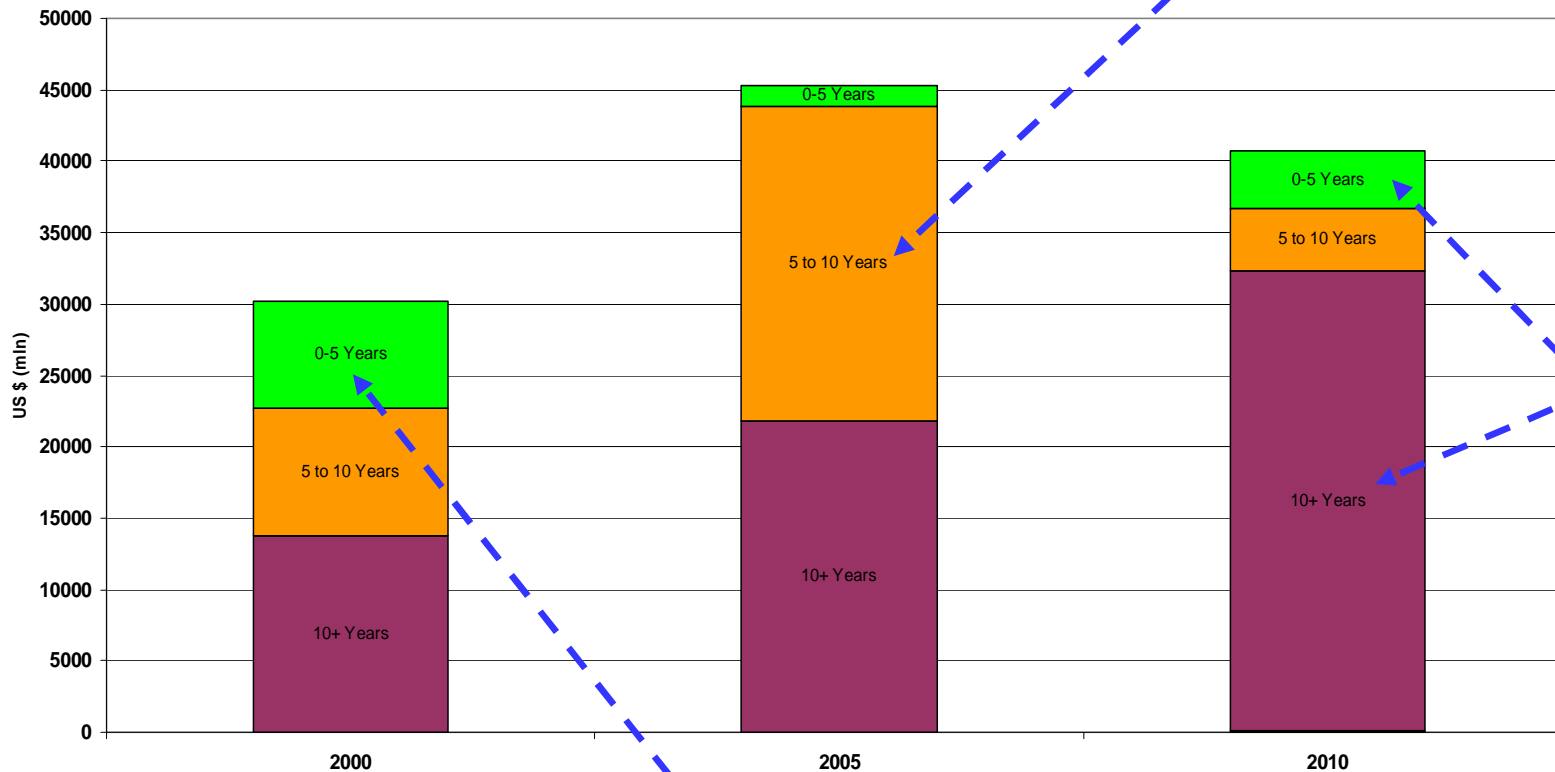
- SG&A is costly in broad CVD market
 - Educational, product launch and promotional expenses are high
 - Sampling and special access programs necessary
 - Large sales force needed to reach a largely PCP market
 - Increasing the influence of the patient
 - Traditional distribution and communication channels are being challenged.
- Increased challenges in developing and commercializing new CVD drugs suggests that only the largest of the large companies can tolerate the risk of going to the broad market.

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Pharma Already has Sufficient Shots on Goal?

Aggregate CVD Sales of Leading Pharma Companies by Product Age



Recent growth driven by mid-life products as fruits of 90s innovation and "fast followers" in a given drug class.

Older products serve as cash cow as new products lag in market penetration.

Rapid growth of truly innovative products into a growing preventative cardiovascular market.

Evaluate Pharma, DH Analysis

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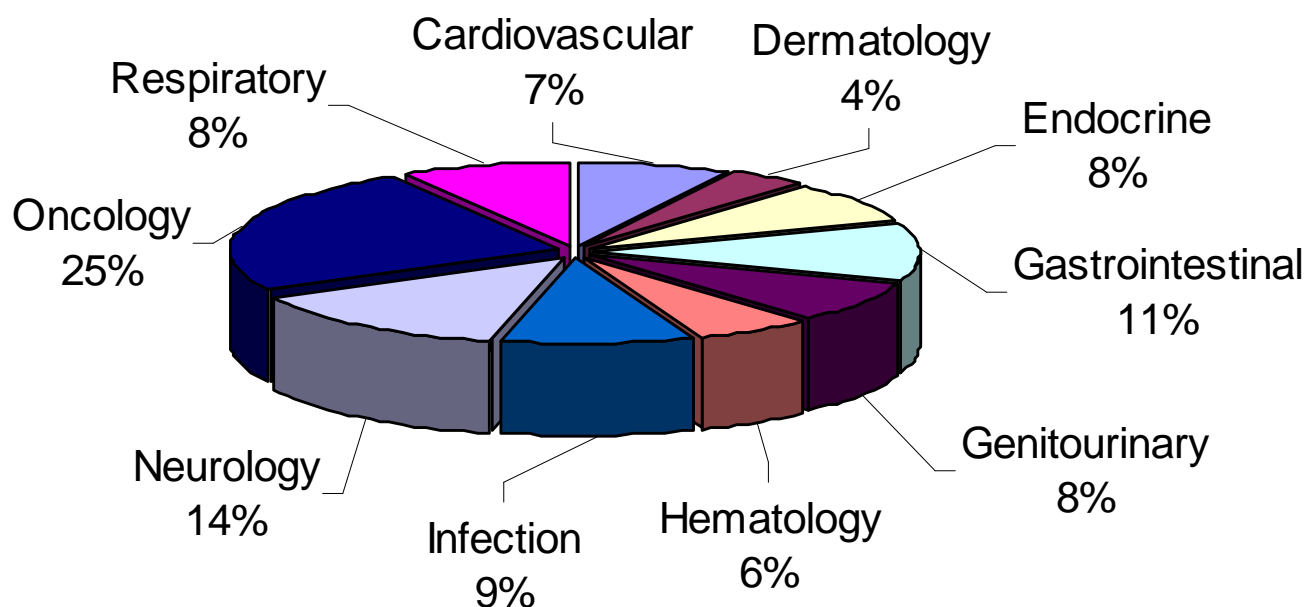
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CVD's Sparse Pipeline

- Although CVD is the largest pharmaceutical market, it represents only 7% of today's clinical stage pipeline.

Clinical Development by Indication



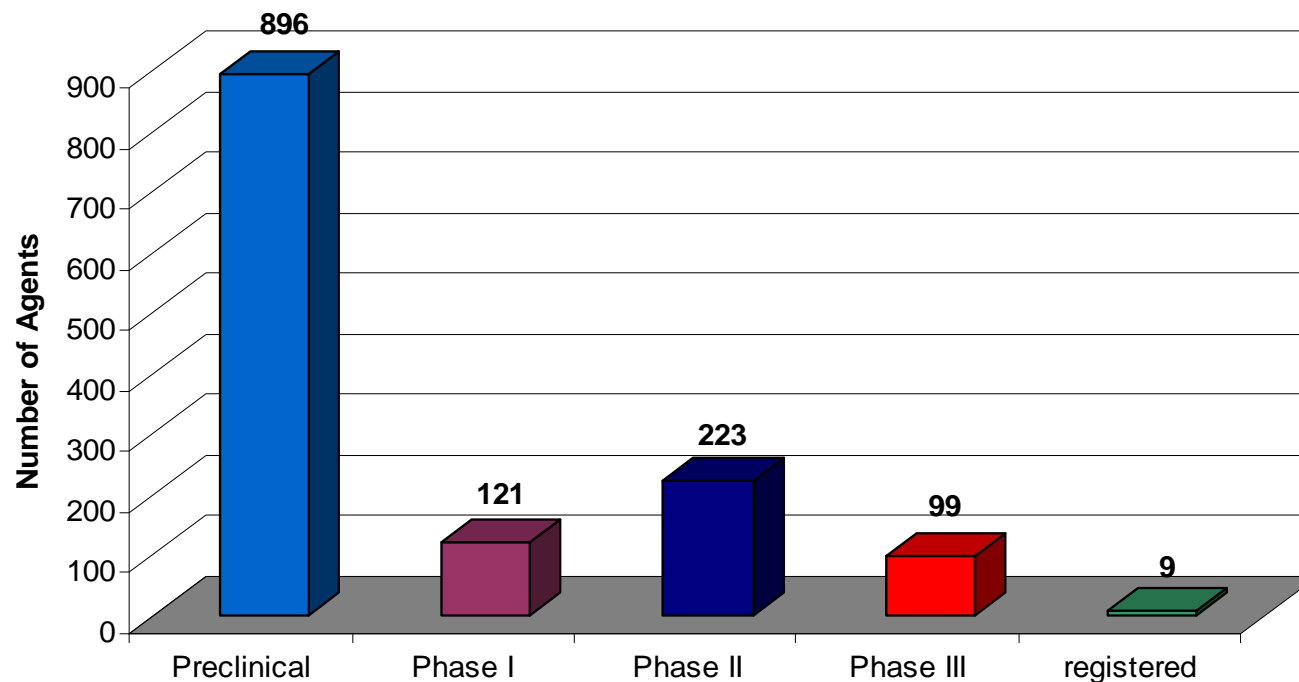
**Pipeline included 6125 pipeline agents in Phase I clinical development to registration.*

Adis R&D Insight, IDdb, DH Analysis

Limited Agents in Development?

- Although development efforts are not in proportion to CVD market size, there are numerous late stage projects in development and, in particular, an active early stage effort.

Cardiovascular Drugs in Development

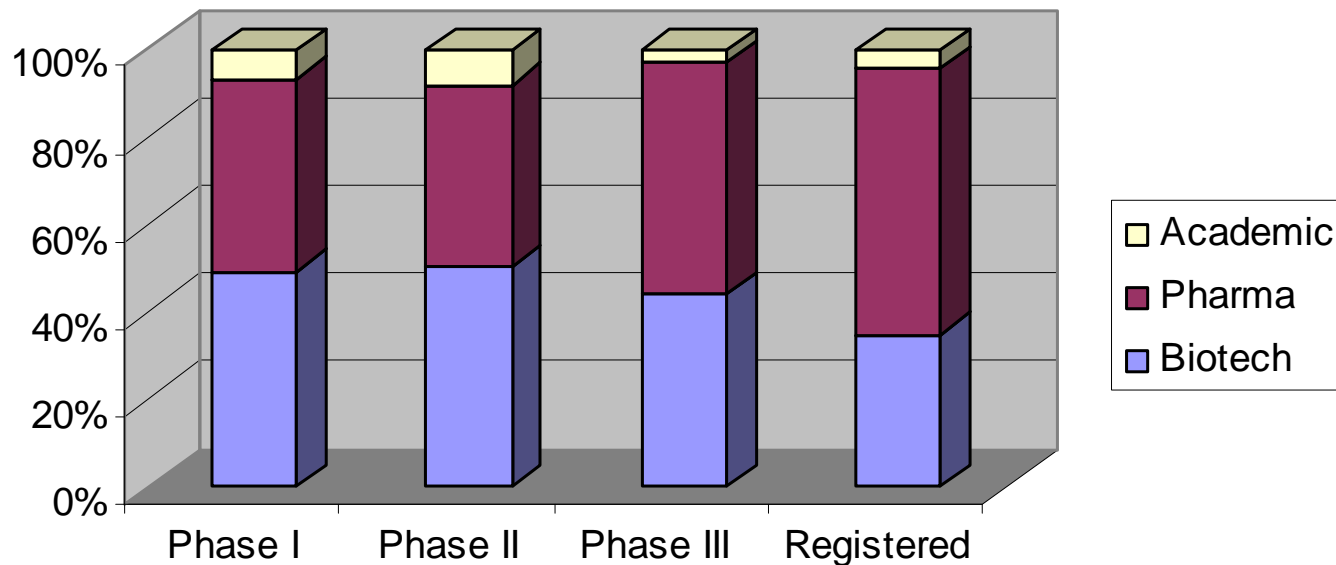


Adis R&D Insight, IDdb, DH Analysis

Too Few CVD Focused Biotechs?

- Actually, a large portion of the current pipeline is sourced from biotech companies

Proportion of CVD Pipeline by Originator



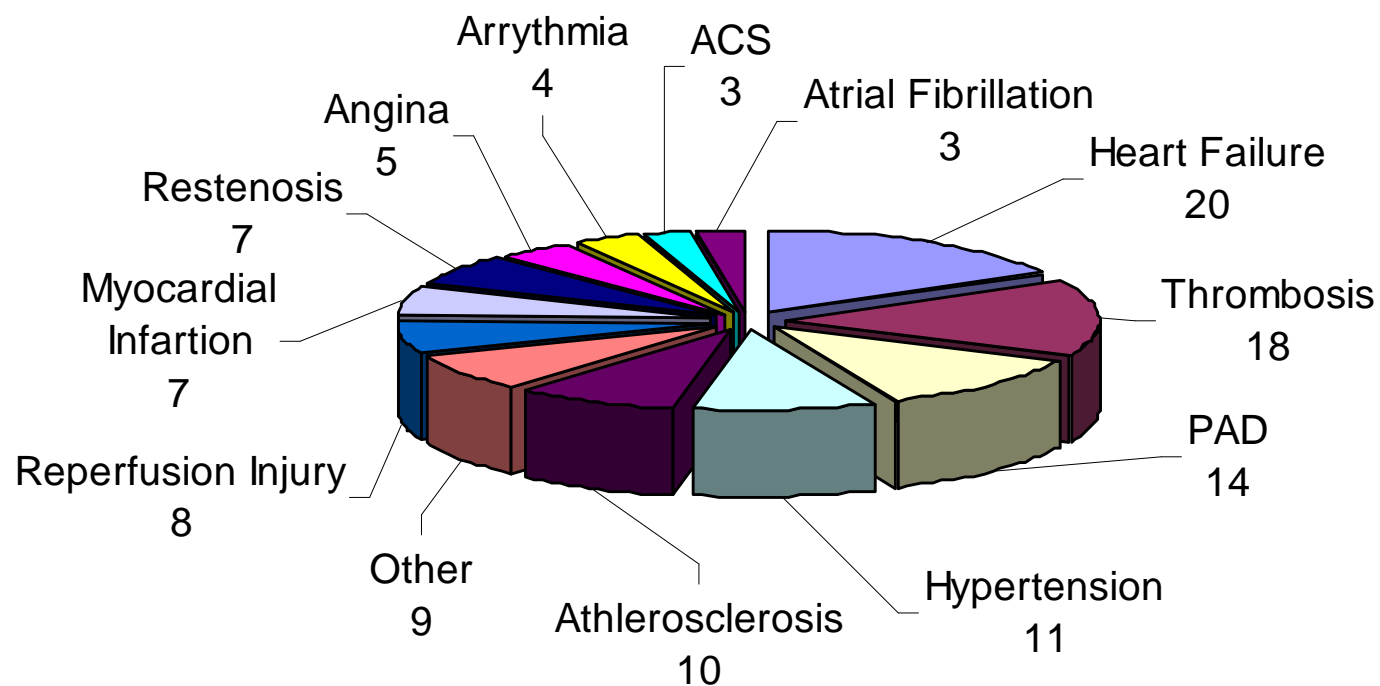
- DH has identified numerous small CV R&D organizations*:
 - There are 104 Biotechs involved in CV development
 - There are 48 Specialty/Regional Pharma in the US, EU and Japan.

* Combining the Evaluate Pharma and BioCentury lists

Adis R&D Insight, IDdb, DH Analysis

CVD “Licensable” Agents

Number of Licensable Agents by Indication



Adis R&D Insight, IDdb, DH Analysis

Windhover's Top 10 Licensable Cardiovascular Projects

Developmental Agent	MOA	Clinical Phase	Indication
<i>CK 1827452 (Cytokinetics)</i>	<i>Cardiac myosin activator</i>	I	Heart Failure
<i>FM-VP4 (Forbes Medi-Tech)</i>	<i>Cholesterol absorption inhibitor</i>	II	Hypercholesterolemia
<i>DG 031 (deCODE genetics)</i>	<i>FLAP inhibitor</i>	III	Myocardial Infarction
<i>ISIS 301012 (Isis Pharmaceuticals)</i>	<i>Apo B100 antagonist</i>	II	Hypercholesterolemia
<i>Acadesine (PeriCor Therapeutics)</i>	<i>Adenosine agonist</i>	III	Myocardial Infarction
<i>MC 1 (Medicure Inc.)</i>	<i>Vitamine B6 metabolite</i>	III	Reperfusion injury
<i>SLX 2101 (Surface Logix)</i>	<i>PDE 5 inhibitor</i>	I	Pulmonary Hypertension
<i>VT 111 (Viron Therapeutics Inc.)</i>	<i>Serine protease inhibitor</i>	II	Coronary Artery Disease
<i>ATI-2042 (ARYx)</i>	<i>Amiodarone analog</i>	II	Atrial fibrillation
<i>Elafin (Proteo Biotech AG)</i>	<i>Leukocyte elastase inhibitor</i>	I	Myocardial Infarction

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