

Science and Technology in Healthcare:

A View From Wall Street

Geoffrey E. Harris, CFA

**Global Head of Healthcare Equity
Research**

November 2000



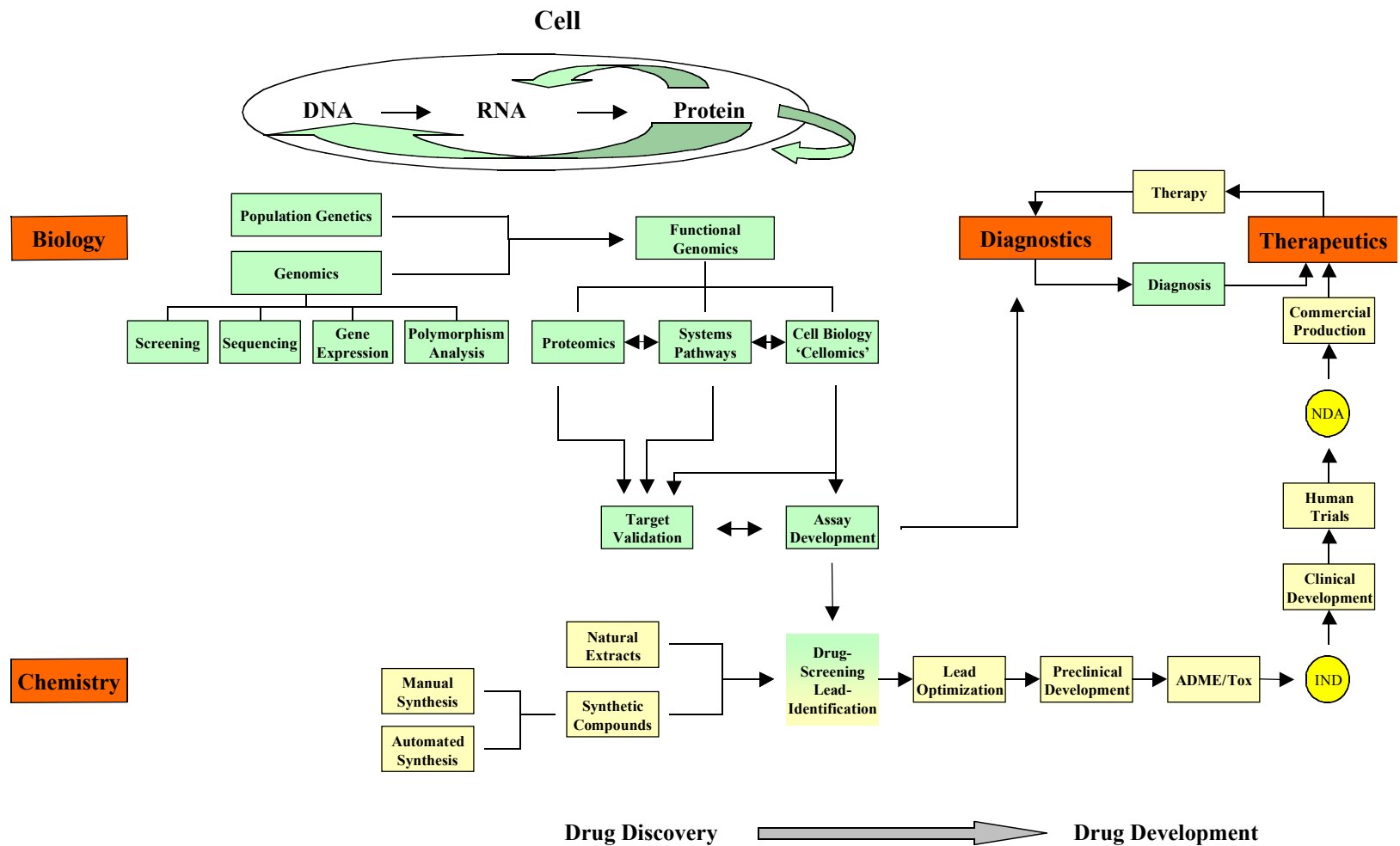
Wall Street allocates fresh capital to segments of the economy experiencing organizational and technological change. New business models and new technologies create opportunities for new organizations to get involved and for old ones to fail.

Two Broad Areas of Change in Healthcare Today:

- ◆ Drug Discovery and Development Process
- ◆ Healthcare Delivery: Diagnostics and Therapeutics

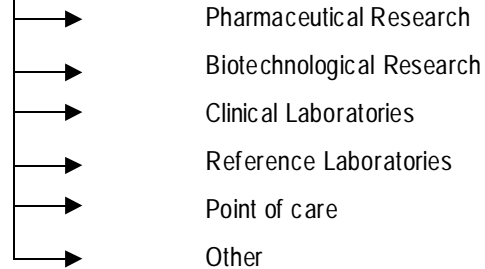
Drug Discovery and Development Process

- ◆ Highly Complex, Multidisciplinary

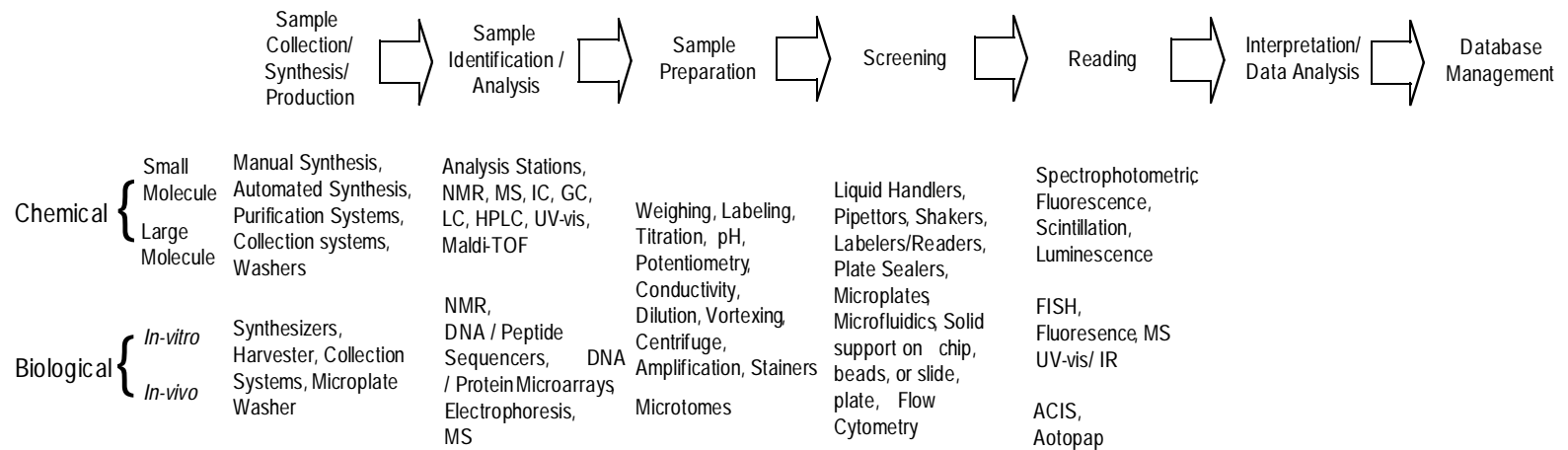


Laboratories are Complex Organizationally and Technically

Laboratory Type



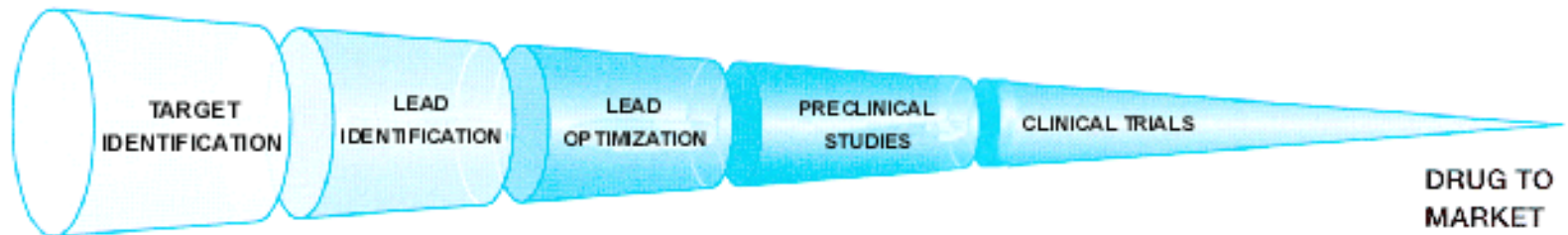
Shared Lab Processes



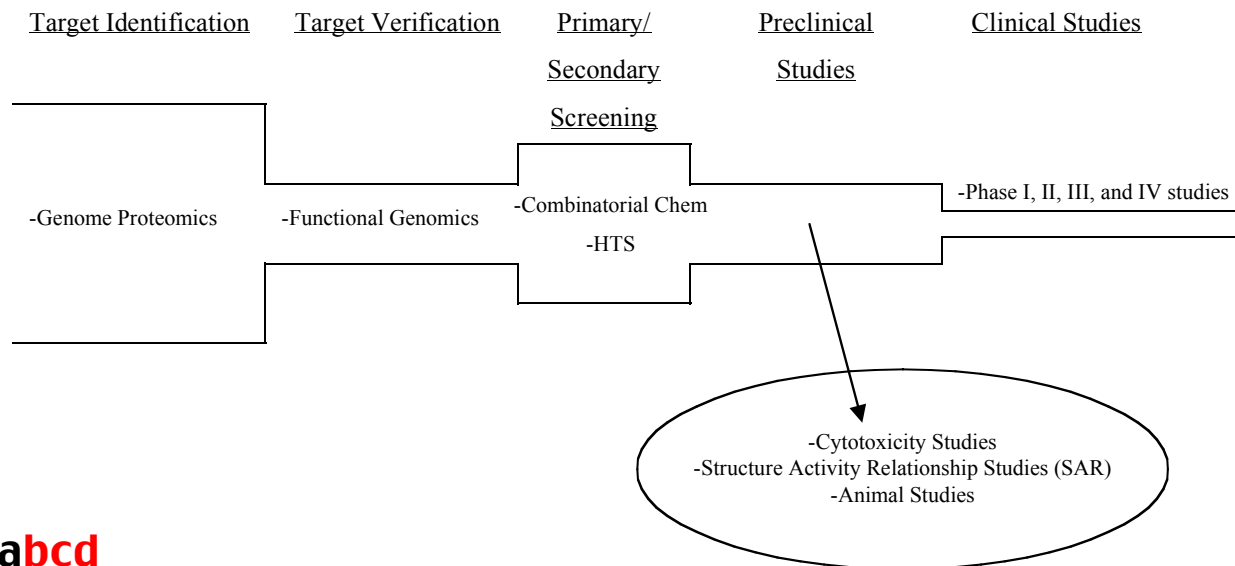
These are largely manual procedures.

Drug Discovery and Development Process:

- ◆ Expensive, Time Consuming, Numerous Bottlenecks



- ◆ \$300 to \$500 million per NCE



Drug Discovery and Development Process:

- ◆ Risky with Low Yields

- 80% failure rate on clinical trials.
- 70% of the drugs that make it through trials fail to recoup their own cost of development.

- ◆ The process is largely chance-based, art-based, luck-based, inspiration-based: unsystematic.

Numerous Patent Expirations:

American Home Products (AHP)

Premarin – expired
Ativan – expired
Cordarone – Expired
Ziac – March 2000
Zosyn/Tazocin – February 2007
Effexor – August 2007

Bristol-Myers Squibb (BMY)

Capoten – Expired
Taxol – Expired (but has limited protection until 2004 due to dosing patents, etc.)
Glucophage – March 2000
Paraplatin – April 2004
Pravachol – October 2005
Zerit – June 2008

Eli Lilly (LLY)

Humulin - Expired
Prozac - 2001 or 2003 (this date is being fought over)
Axid - 2002
Gemzar - 2006
Zyprexa - 2011
Evista – 2013

Johnson & Johnson (JNJ)

Monistat – Expired
Retin-A - Expired
Ortho-Cept - Expired
Nizoral - 1999
Hismanal – 1999
Sporanox – 2000
Ultram - 2000
Terazol – 2001
Floxin - 2003
Ortho-Novum – 2003
Ortho Tri-Cyclin – 2003
Duragesic – 2004
Procit – 2004 (compound patent) & 2012 (manufacturing patent)
Regranex - 2006
Propulsid - 2007
Levaquin - 2010
Risperdal - 2010

Merck (MRK)

Vasotec - 2000
Pepcid - 2000
Mevacor - 2001
Prinivil - 2001
Zocor - 2005
Fosamax - 2007
Cozaar/Hyzaar - 2009
Crixivan - 2013

Pfizer (PFE)

Procardia – Expired
Cardura – 2000
Diflucan – 2004
Zithromax – 2005
Zolof – 2005
Norvasc – 2007
Trovan – 2009
Lipitor - 2010 (co-promoting with Warner-Lambert)
Viagra - 2011

Schering-Plough (SGP)

Imdur – Expired
Vancenase – 1999
Intron A/Rebetron – 2002/2015 (the later date for Rebetron)
Fareston – 2004
Claritin – 2002 (composition of matter) or 2004 (based on its metabolite but numerous patent extensions such as combinations with decongestants pushes some of the patent expiration dates out to 2012)
K-Dur – 2006

Warner-Lambert (WLA)

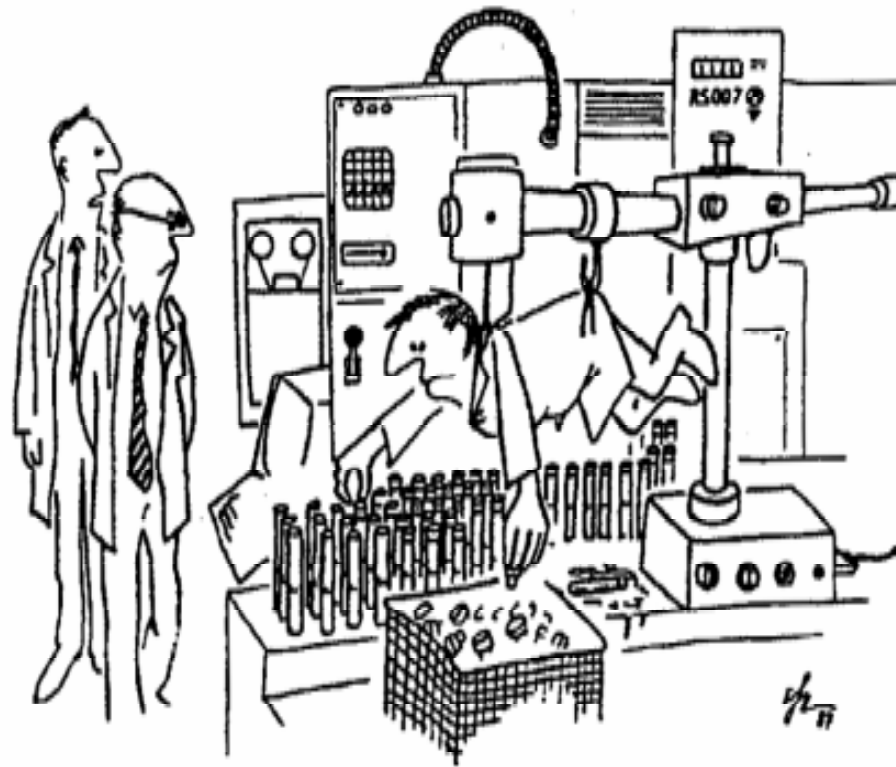
Dilantin - Expired
Loestrin - Expired
Neurontin - 2000
Accupril - 2002
Rezulin - 2008
Lipitor - 2010

Source: www.labpuppy.com

Bottom Line: Enormous pressure/opportunity to improve R&D productivity and to reduce risk.

Solutions:

- ◆ Automation



"We were able to remove some initial difficulties this way"

Solutions

◆ Industrial Scale

- In a single day, the Whitehead Institute generates 50 million bases of DNA Sequence.
- deCODE genetics just ordered 50 DNA sequencers from Applied Biosystems (PEB).
- Geneva Proteomics just ordered 51 Mass Spectrometers from Bruker Daltonics.

Solutions

- ◆ Data mining versus hypothesis-based science.
- ◆ Drive to systematize science from art to engineering.

Solutions

- ◆ Each of these solutions requires capital investment on an unprecedented scale.
 - Technology
 - Informatics
 - IP
 - Infrastructure

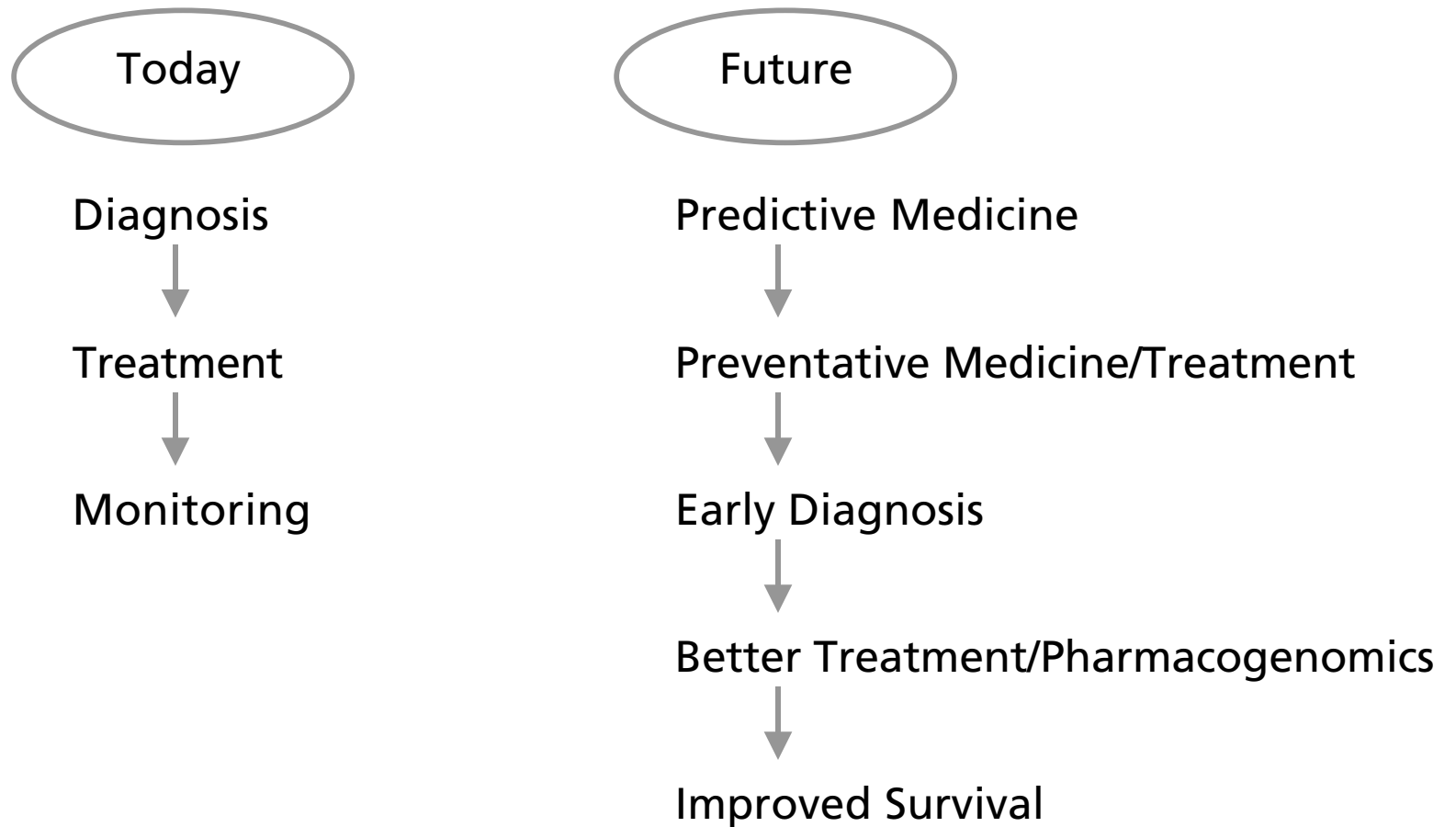
Solutions

- ◆ Investors are betting that these investments in improving the R&D process will yield more, and more profitable, therapeutics with less risk.

Solutions

- ◆ These solutions also require new business models:
 - Outsourcing
 - Virtual Companies
 - Multidisciplinary
 - Aggregators of Information
- ◆ Investors are betting on new organizational structures.

Healthcare Delivery: Diagnostics and Therapeutics



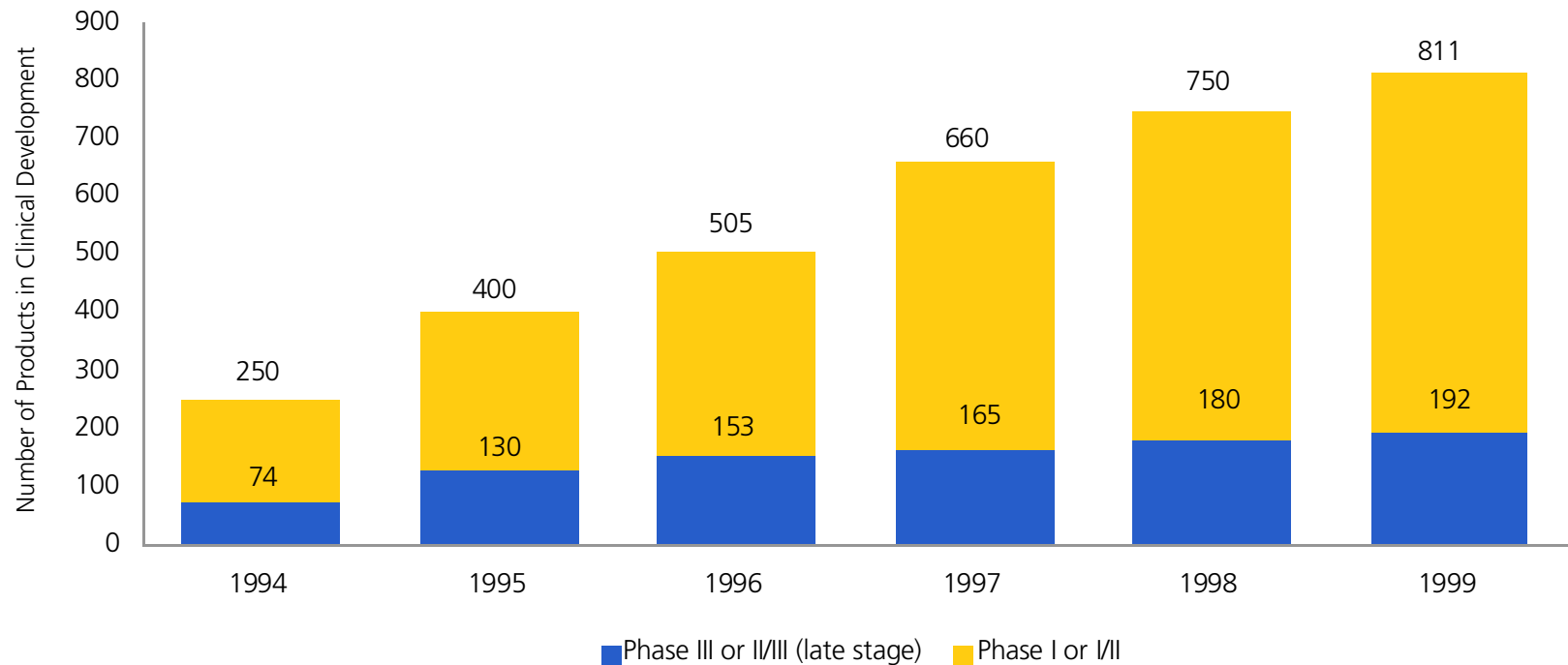
Trends

- ◆ Spending and investment shifts from healthcare services and traditional therapies to molecular diagnostics and new biotechnology therapeutics.
- ◆ Capital flows are proceeding these shifts.

The Score Card

Reality and Wall Street

Biotechnology Pipeline Continues to Grow



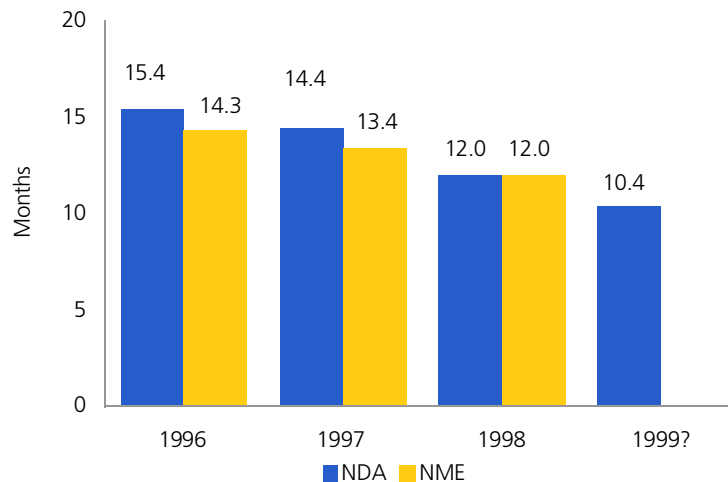
SOURCE: UBS Warburg estimates

Biotechnology Pipeline Continues to Grow

◆ Explosion of Biotech Products

- 1998/99 were years with a record number (over 20 each year) of biotechnology product approvals.
- Currently, there are more Phase III products in development than ever before.
- Biotechnology pipeline rivals the pharmaceutical pipeline for quality and quantity.

**Avg. Number of Months
for a Drug to Receive FDA Approval**



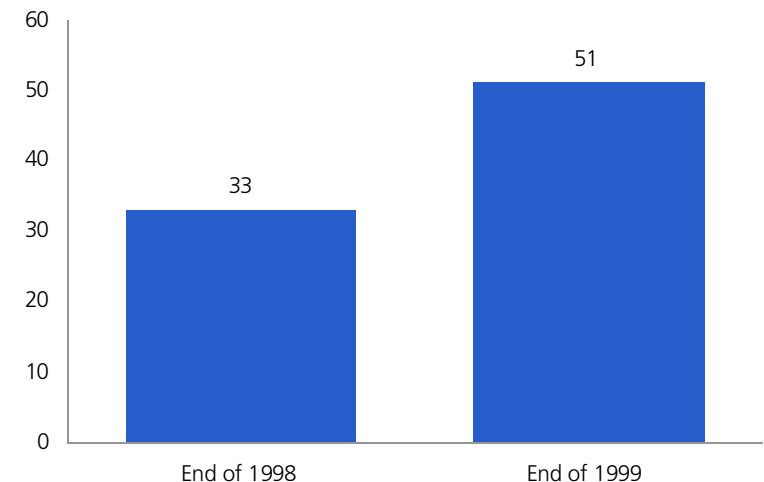
SOURCE: FDA and UBS Warburg LLC

NOTE: 1999 data include only biotech drugs

◆ Driving Overall Enthusiasm

- Flagship products continue strong growth (e.g. Epogen, Cerezyme, Avonex).
- Recently launched products exceed expectations (e.g. Synagis, Rituxan, Herceptin, Enbrel).
- New products continue to offer good sales promise (e.g. Anti-IgE, Anti-CD11a, C225).

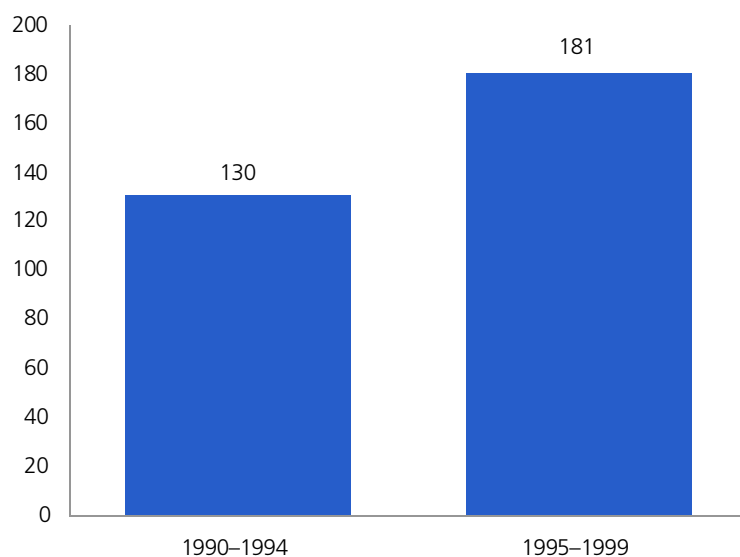
**Cumulative Number of NDAs Filed by
Biotech Companies that have yet to Receive FDA Approvals**



SOURCE: UBS Warburg LLC records and data from FDA

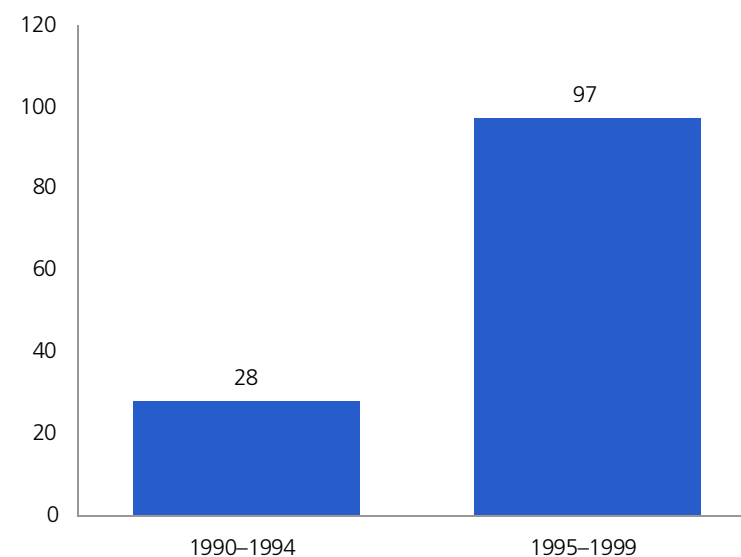
Increasing Pace of Regulatory Approvals

Approved New Chemical Entities



SOURCE: UBS Warburg

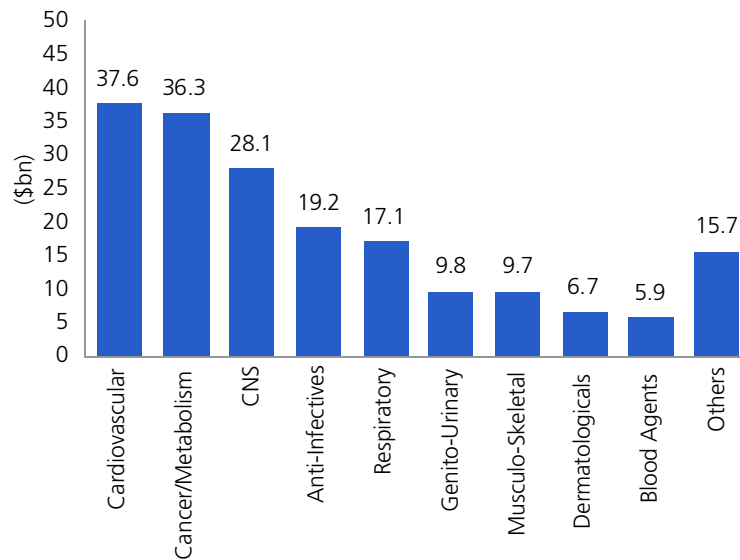
New Biotechnology Products



SOURCE: UBS Warburg

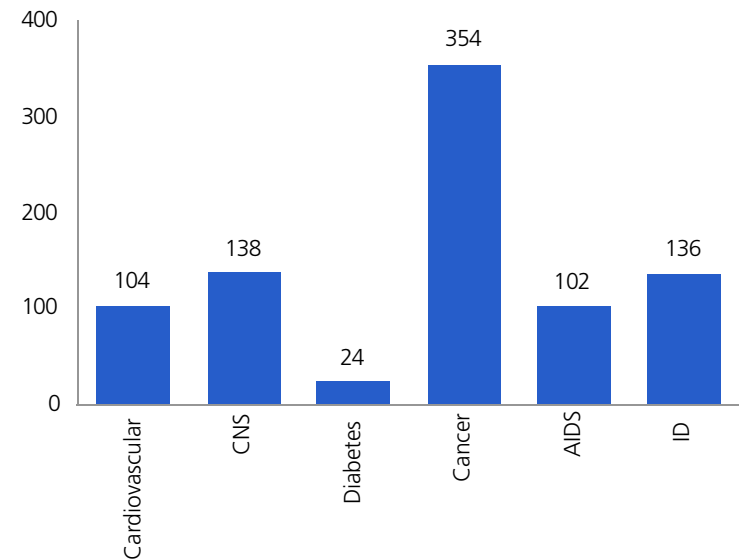
Significant Product Pipeline in Biotech Companies

1998 Pharmaceutical Sales in Various Therapeutic Areas



SOURCE: IMS Health International

Products in Development for Different Therapeutic Areas

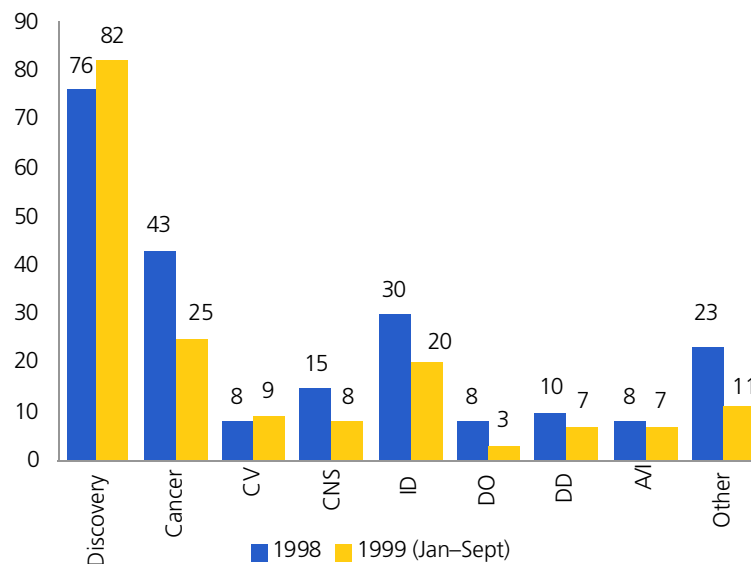


SOURCE: PhMRA and UBS Warburg LLC

Discovery of Drug Candidates was the “Hot” Sector

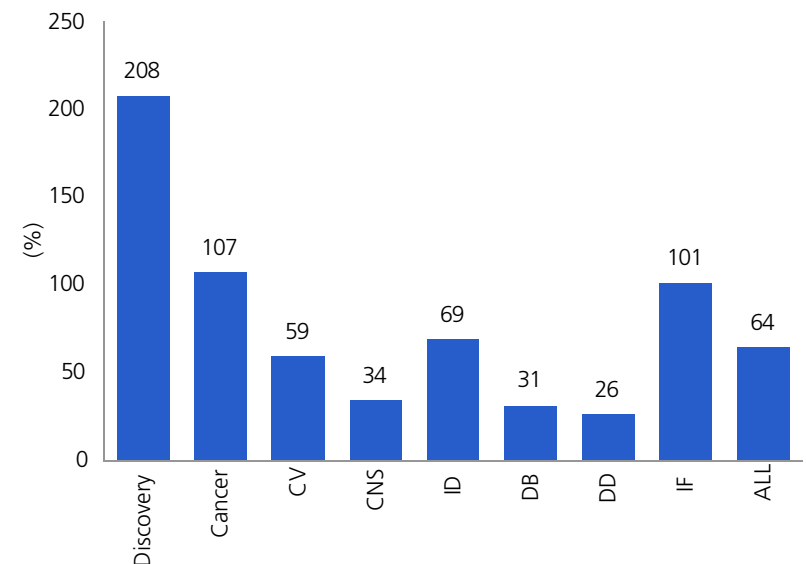
◆ 1999-2000 YTD

Big Pharma-Biotech Alliances



SOURCE: BioCentury and UBS Warburg LLC

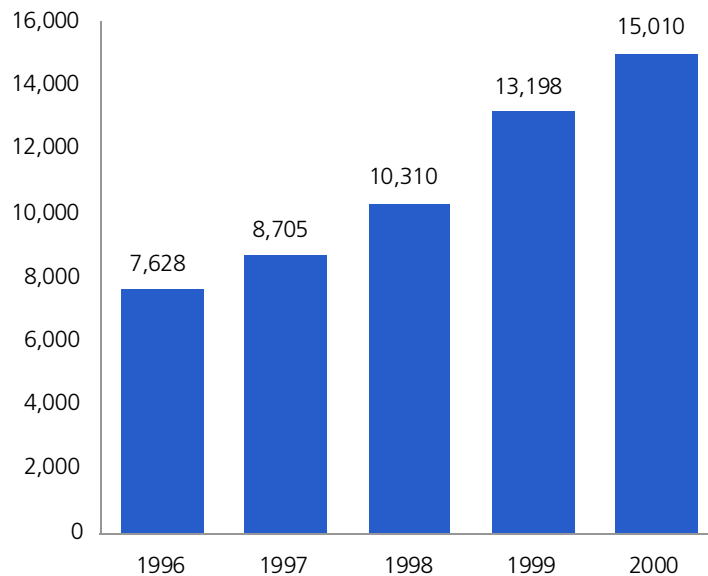
Performance of Biotech Companies in Different Categories



SOURCE: BioCentury and UBS Warburg LLC

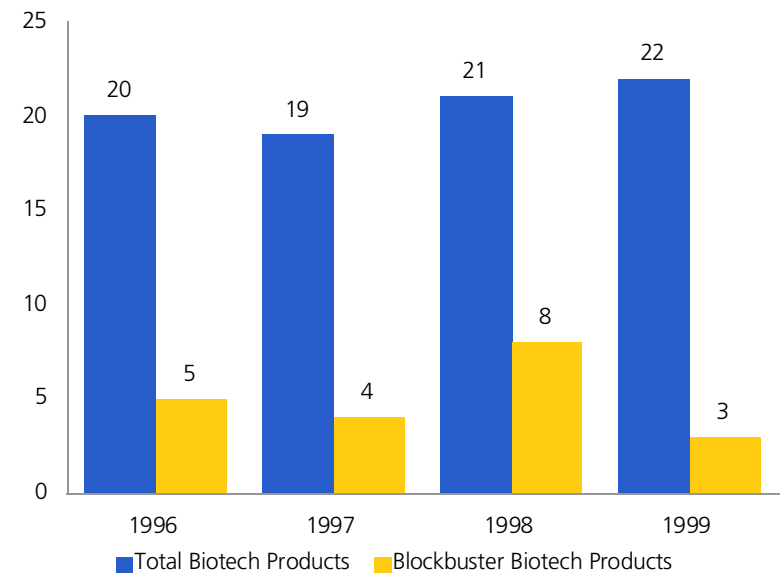
Biotechnology Industry Outlook-- Product Sales

Key Biotech Product Sales



SOURCE: UBS Warburg LLC estimates

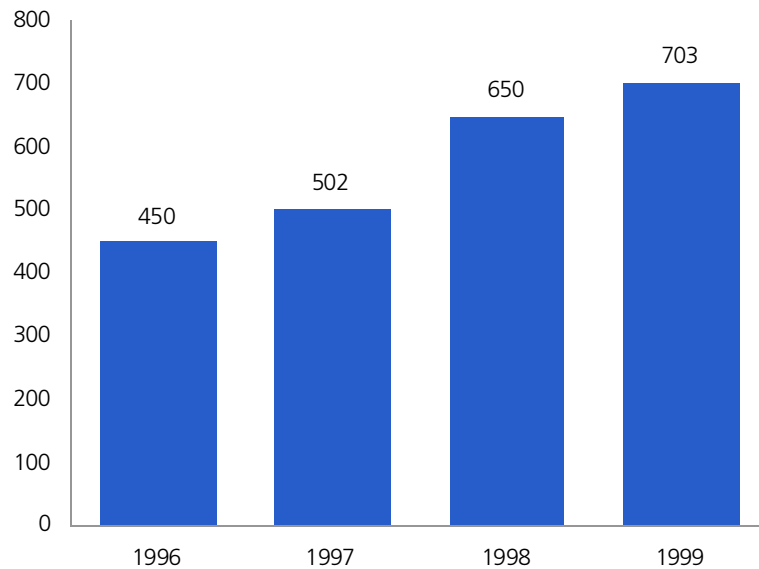
Biotech Products Reach the Marketplace



SOURCE: FDA and UBS Warburg LLC estimates

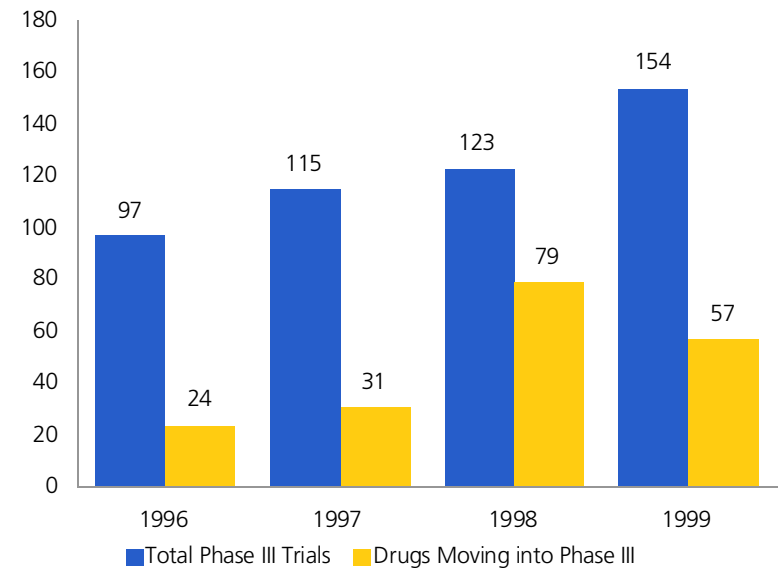
Biotechnology Industry Outlook-- Product Pipeline

Total Biotech Clinical Trials



SOURCE: UBS Warburg LLC estimates

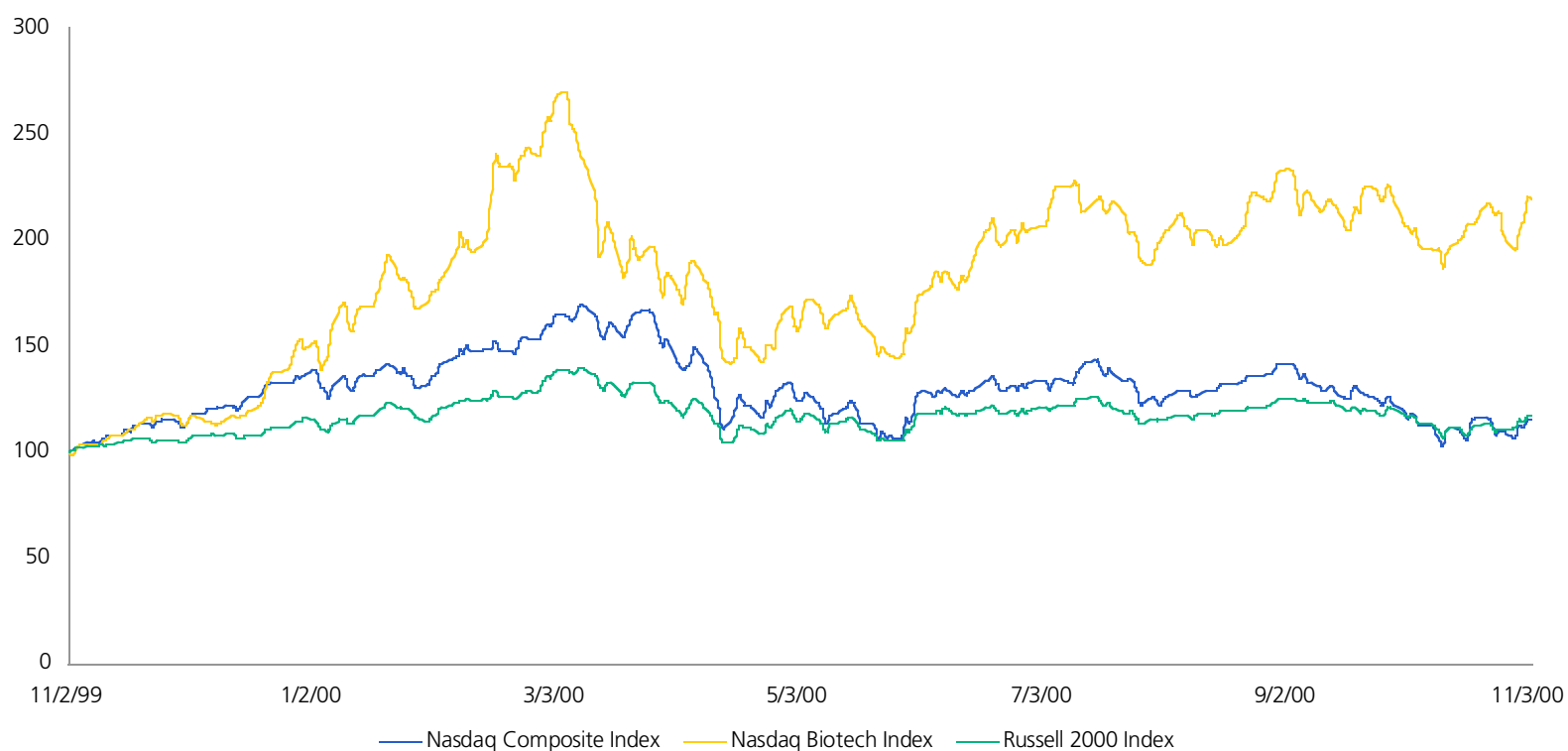
Biotech Phase III Trials



SOURCE: UBS Warburg LLC estimates

Wall Street Indicators

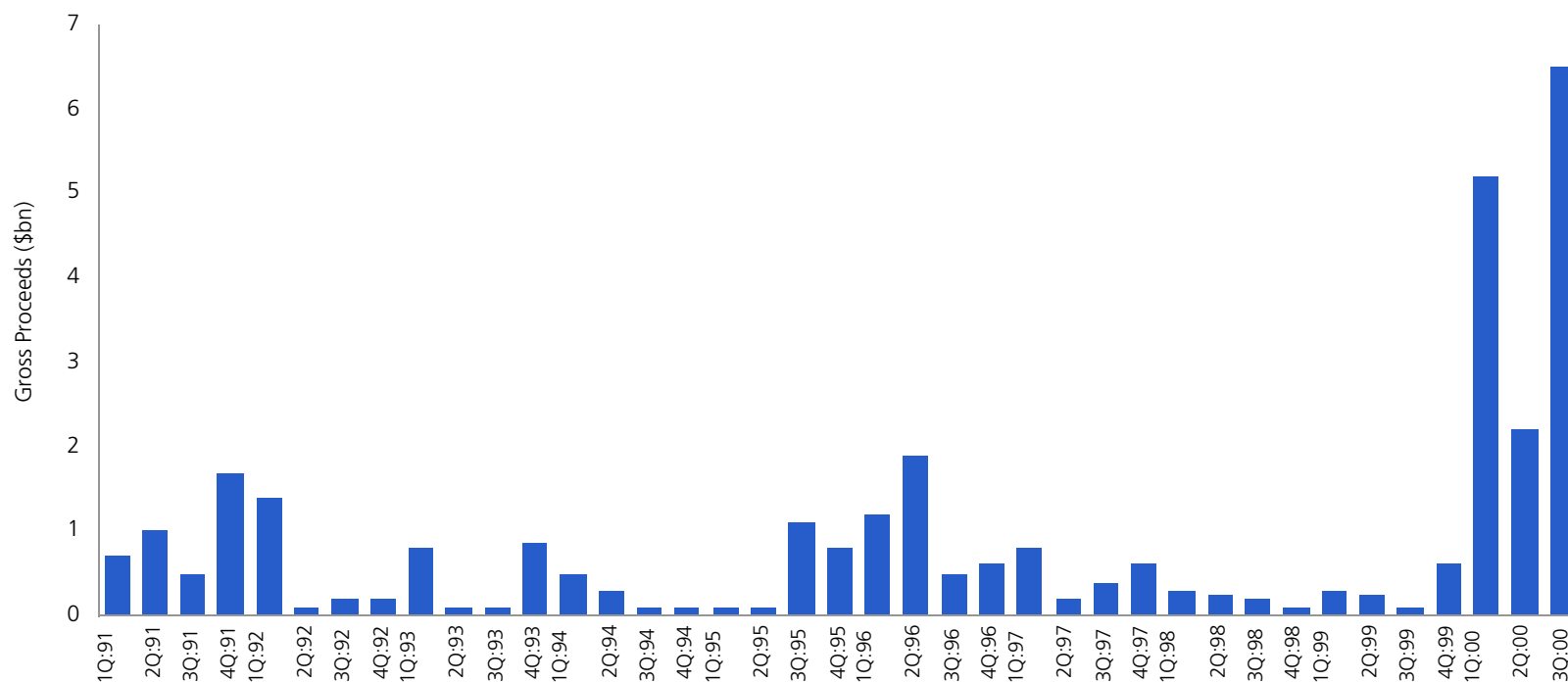
◆ Biotechnology/Life Sciences Market Conditions



SOURCE: FactSet

Wall Street Indicators

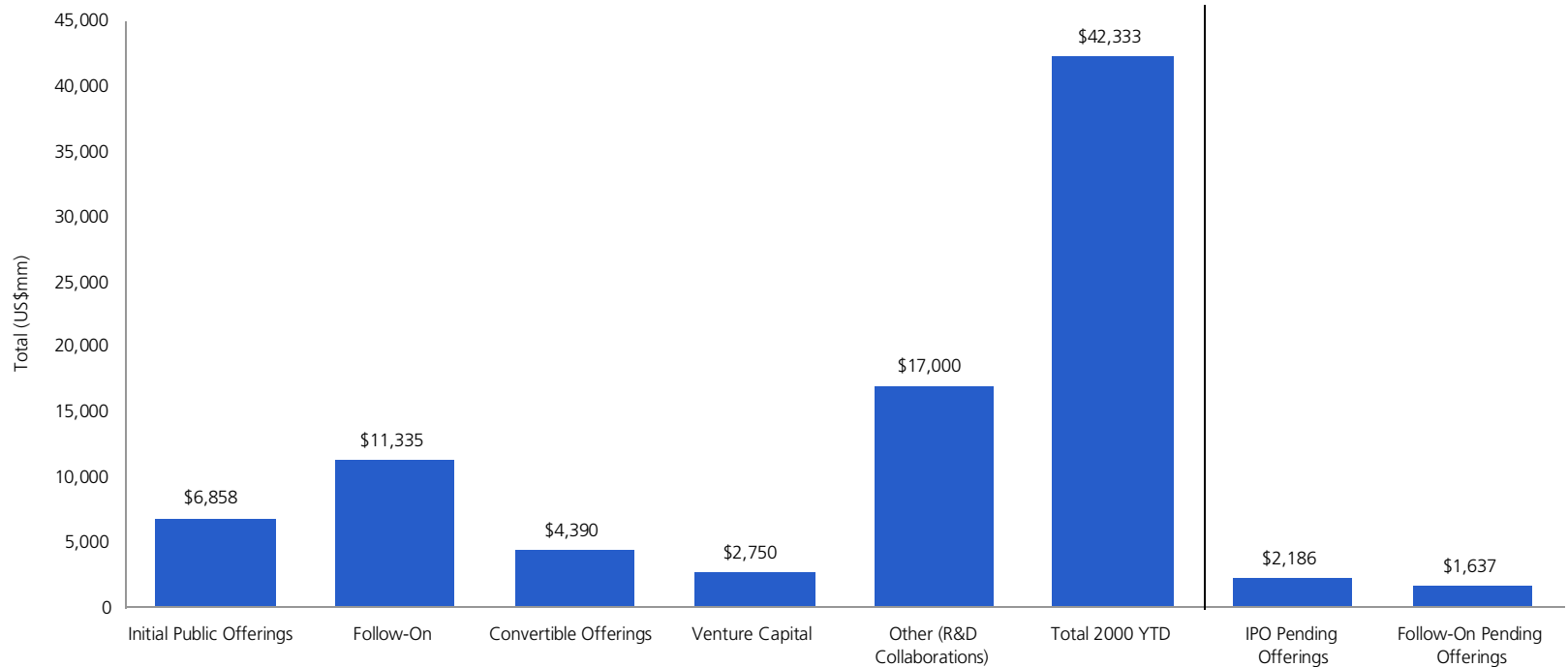
◆ Gross Proceeds for Biotech Public Stock Offerings (Initial and Follow-On Offerings Combined)



SOURCE: UBS Warburg LLC

Wall Street Indicators

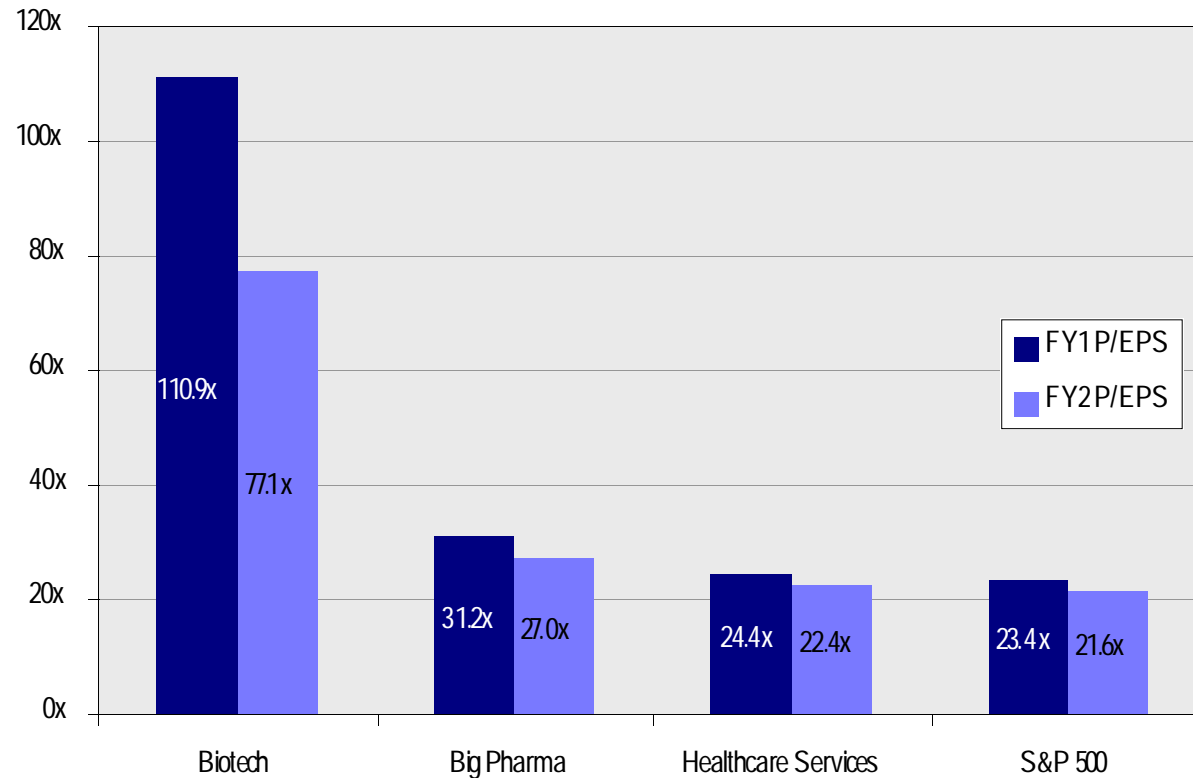
◆ Equity Investments in Biotech/Life Sciences 2000 (January-October 2000 Public/Private Offerings)



SOURCE: UBS Warburg LLC estimates

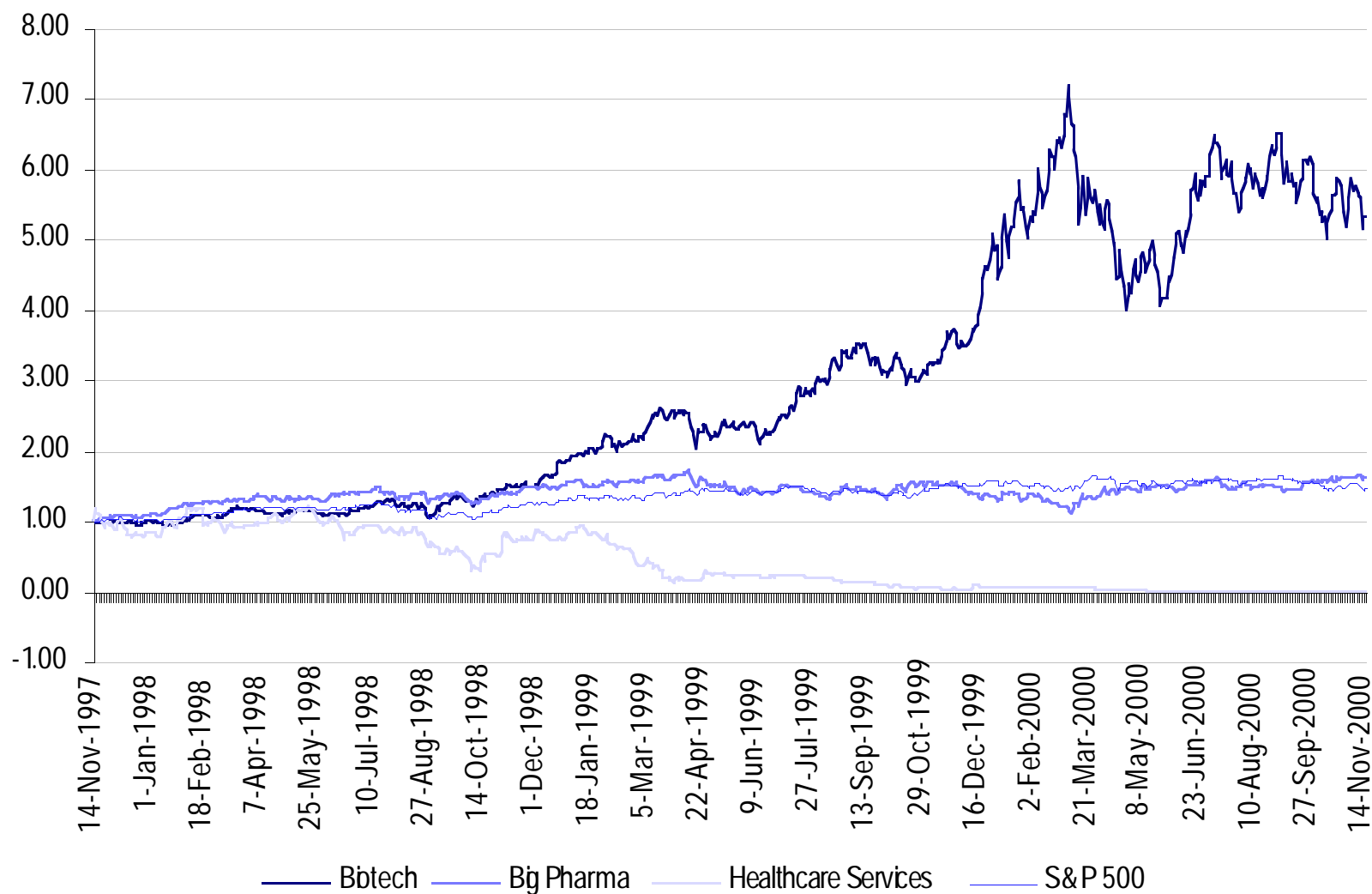
- ◆ An awe-inspiring amount of money has been invested in biotech in 2000 YTD (over \$42 billion), in contrast with \$12.4 billion in 1999 (\$2.8 billion in IPOs, \$4.2 billion in follow-ons, \$1.8 billion in venture capital, and \$3.6 in other fund raising)

Wall Street Indicators



- ◆ Biotechnology capital costs are low, on a P/EPS basis compared to Big Cap Pharma, Healthcare Services, and the S&P 500, reflecting investor expectations of high future returns on the investments they are making today and lower perceived risk.

Wall Street Indicators



Who We Are:

A Leader in
Healthcare Financing
and M&A

UBS Warburg--Healthcare Transaction Rankings

◆ Full Credit to Bookrunning Manager

Global Initial Public Offerings
Ranking by Number of Transactions
Completed
January 1, 2000–Present

Bookrunning Manager	No. of	
UBS Warburg	18	1,744
BB–Robertson	9	584
Lehman Brothers	8	708
Chase H&Q	8	460
DB Alex. Brown	7	868
Merrill Lynch	6	707
CS First Boston	5	729
...

January 1, 1999–Present

Global Equity & Equity-Linked Offerings
Ranking by Number of Transactions
Completed
January 1, 2000–Present



January 1, 1999–Present



Global Straight Debt Offerings
Ranking by Number of Transactions
Completed
January 1, 2000–Present



January 1, 1999–Present



Global M&A Transactions
Ranking by Number of Transactions
Announced and Completed
January 1, 2000–Present



January 1, 1999–Present



UBS Working Performance of Health Care Equity Offerings

UBS Warburg--Performance of Healthcare IPOs

◆ Leadership in Quality while Dominating Market Share

January 1, 2000 to Present ¹

All Lead Managed Healthcare Equity Offerings Above Issue Price

Rank	Bookrunning Manager	No. of Deals Up	Total No. of Deals	Batting Average
1	Bear Stearns	4	4	1.000
2	Credit Suisse First Boston	10	11	0.909
3	CIBC	6	7	0.857
4	Lehman Brothers	9	11	0.818
5	ING Barings	3	4	0.750
6	Salomon Smith Barney	6	8	0.750
7	UBS Warburg	17	24	0.708
8	DLJ	4	6	0.667
9	Morgan Stanley Dean Witter	8	12	0.667
10	Prudential Vector	4	6	0.667
11	DB Alex. Brown	5	8	0.625
12	BB-Robertson	8	13	0.615
13	US Bancorp Piper Jaffray	3	5	0.600
14	Merrill Lynch	7	12	0.583
15	JP Morgan	5	9	0.556
16	Chase H&Q	5	10	0.500
17	SG Cowen	2	5	0.400
18	Goldman Sachs	3	9	0.333
19	Banc of America	1	4	0.250

Performance of All Lead Managed Healthcare Equity Offerings

Rank	Bookrunning Manager	Total No. of Deals	Weighted Average of % Change Offer to Current
1	DLJ	6	52.4
2	Bear Stearns	4	42.5
3	UBS Warburg	24	41.1
4	Credit Suisse First Boston	11	39.7
5	Lehman Brothers	11	36.0
6	BB-Robertson	13	30.7
7	DB Alex Brown	8	29.4
8	CIBC	7	21.9
9	US Bancorp Piper Jaffray	5	20.7
10	Merrill Lynch	12	13.7
11	Banc of America	4	7.2
12	SG Cowen	5	5.3
13	ING Barings	4	2.8
14	Salomon Smith Barney	8	2.4
15	Chase H&Q	10	(4.3)
16	Morgan Stanley Dean Witter	12	(8.6)
17	Prudential Vector	6	(13.1)
18	JP Morgan	9	(14.7)
19	Goldman Sachs	9	(27.4)

SOURCE: SDC/FactSet

NOTE: 1 As of 10/31/00

UBS Warburg--Performance of Healthcare IPOs

◆ Leadership in Quality while Dominating Market Share

January 1, 2000 to Present¹

All Lead Managed Healthcare IPOs Above Issue Price

Rank	Bookrunning Manager	No. of Deals Up	Total No. of Deals	Batting Average
1	US Bancorp Piper Jaffray	3	3	1.000
2	Bear Stearns	3	3	1.000
3	Prudential Vector	1	1	1.000
4	ING Barings	1	1	1.000
5	Salomon Smith Barney	4	4	1.000
6	Lehman Brothers	7	8	0.875
7	Morgan Stanley Dean Witter	4	5	0.800
8	CIBC	4	5	0.800
9	Credit Suisse First Boston	3	4	0.750
10	UBS Warburg	12	17	0.706
11	Merrill Lynch	4	6	0.667
12	DLJ	2	3	0.667
13	JP Morgan	3	5	0.600
14	Goldman Sachs	3	5	0.600
15	DB Alex. Brown	4	7	0.571
16	BB-Robertson	5	9	0.556
17	Chase H&Q	3	7	0.429
18	SG Cowen	2	5	0.400
19	Banc of America	0	1	0.000

Performance of All Lead Managed Healthcare IPOs

Rank	Bookrunning Manager	Total No. of Deals	Weighted Average of % Change Offer to Current
1	ING Barings	1	94.1
2	Credit Suisse First Boston	4	69.2
3	Prudential Vector	1	63.8
4	Salomon Smith Barney	4	58.7
5	Merrill Lynch	6	54.2
6	DLJ	3	52.9
7	UBS Warburg	17	46.6
8	Lehman Brothers	8	38.7
9	US Bancorp Piper Jaffray	3	38.1
10	Bear Stearns	3	34.6
11	DB Alex Brown	7	32.1
12	Morgan Stanley Dean Witter	5	26.5
13	JP Morgan	5	23.2
14	Goldman Sachs	5	22.0
15	BB-Robertson	9	19.6
16	Chase H&Q	7	16.4
17	CIBC	5	13.1
18	SG Cowen	5	5.3
19	Banc of America	1	(9.4)

SOURCE: SDC/FactSet

NOTE: 1 As of 10/31/00

UBS Warburg--Global Biotech Sector Rankings

◆ Full Credit to Bookrunning Manager

Global Initial Public Offerings

Ranking by Number of Transactions Completed
January 1, 2000–Present

Bookrunning Manager	No. of	(US\$mm)
UBS Warburg	15	1,390
Lehman Brothers	7	656
CIBC	6	918
DB Alex. Brown	6	820
BB-Robertson	6	459
Chase H&Q	6	376

Global Equity and Equity-Linked Offerings

Ranking by Number of Transactions Completed
January 1, 2000–Present

--

Global M&A Transactions

Ranking by Number of Transactions Announced and Completed
January 1, 2000–Present

--

“

“For four years, the biotech market was incubating in venture capital,” said Benjamin Lorello, managing director of global health-care investment banking for **UBS Warburg, which has underwritten more biotech IPOs than any other firm**. “What looks to the outside world as a never-ending stream is a backlog of quality that was building up.”

UBS Warburg has underwritten \$412 million worth of biotech IPOs this year—representing 17% of all initial offerings in the sector, according to Bloomberg analytics.

J.P. Morgan has underwritten \$305 million in biotech IPOs, about 13%, and Goldman Sachs is third with 9% and \$214.3 million.

”

BLOOMBERG, "BIOTECH OFFERINGS POUR INTO MARKET FOR A BANNER IPO SEASON" BY ANGELA ZIMM
August 11, 2000

UBS Warburg--Biotech IPO Performance

◆ Lead Managed Equity Transactions 1999 to Present

Offer Date	Issuer	UBS Warburg Role	Gross Proceeds (\$mm)	% Change in Price since Offer	
				1 Day After (%)	11/10/00 (%)
10/25/00	MediChem Life Sciences Inc	Bookrunning Manager	52.8	0.35	0.59
10/11/00	Genmab	Bookrunning Manager	181.8	(0.34)	(1.97)
10/6/00	IsoTis BV	Bookrunning Manager	70.6	(0.58)	(1.43)
9/28/00	Starpharma Pooled Development	Bookrunning Manager	12.2	(0.05)	(0.11)
9/22/00	Genesis Research and Development	Bookrunning Manager	14.2	0.08	0.21
9/15/00	Lambda Physik AG	Bookrunning Manager	181.8	8.38	6.97
8/4/00	Bruker Daltonics	Bookrunning Manager	119.6	6.08	14.41
7/31/00	Pharmagene Plc	Bookrunning Manager	76.9	0.19	(0.40)
7/19/00	Argonaut Technologies	Bookrunning Manager	79.4	2.91	1.21
6/20/00	Cepheid	Bookrunning Manager	34.5	1.13	1.29
5/5/00	Genomic Solutions	Bookrunning Manager	61.3	0.19	1.41
3/30/00	Luminex	Bookrunning Manager	76.5	1.74	5.78
3/24/00	Intermune	Bookrunning Manager	125.0	2.05	9.77
3/21/00	Aclara Biosciences	Joint Bookrunning Manager	217.4	7.54	12.07
1/31/00	Sequenom	Bookrunning Manager	157.0	21.04	0.00
11/9/99	Evotec Biosystems AG	Bookrunning Manager	67.0	2.73	17.20
		Average	95.5	3.3	4.2
		Median	76.7		
		Total	1528.0		

UBS Warburg--Biotech Follow-On Performance

◆ Lead Managed Equity Transactions 1999 to Present

Offer Date	Issuer	UBS Warburg Role	Gross Proceeds (\$mm)	Change in Price since Offer	
				1 Day After (%)	11/10/00 (%)
4/7/00	Corixa Corp	Bookrunning Manager	64.0	0.70	2.45
3/29/00	Oxford Asymmetry	Bookrunning Manager	52.0	0.04	1.98
3/16/00	Nanogen	Bookrunning Manager	82.5	(1.30)	(6.41)
2/10/00	Ares-Serono S.A.	Joint Bookrunning Manager	564.1	1.56	42.92
2/4/00	Genzyme Transgenics	Bookrunning Manager	80.5	2.23	(1.20)
9/30/99	Connetics	Bookrunning Manager	24.0	0.14	0.38
6/1/99	Tecan AG	Bookrunning Manager	57.0	0.12	19.60
Average			132.0	0.5	8.5
Median			64.0		
Total			924.1		

UBS Warburg--Aftermarket Support

◆ All Lead Managed Biotechnology Transactions (Time period: from date of IPO or follow-on to present)

Aclara Biosciences Inc. (IPO)

March 21, 2000 to Present

Broker	Volume	(%)
DB Alex Brown	27,238	49.69
U.S. Bancorp Piper Jaffray	6,139	11.20
UBS Warburg	4.252	7.76

Ares-Serono

February 10, 2000 to Present



Argonaut Technologies Inc. (IPO)

July 19, 2000 to Present



Bruker Daltonics (IPO)

August 4, 2000 to Present



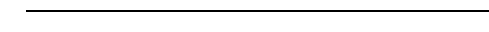
Cepheid (IPO)

June 20, 2000 to Present



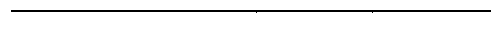
Connetics Corp.

September 30, 1999 to Present



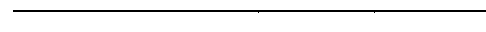
Corixa

April 7, 2000 to Present



Evotec Biosystems AG (IPO)

November 9, 1999 to Present



Genomic Solutions Inc. (IPO)

May 5, 2000 to Present



UBS Warburg--Aftermarket Support (continued)

◆ All Lead Managed Biotechnology Transactions (Time period: from date of IPO or follow-on to present)

Genzyme Transgenics

February 4, 2000 to Present

Broker	Volume	(%)
PaineWebber	12,072	17.31
UBS Warburg	7,587	10.88
Credit Suisse First Boston	6,235	8.94

InterMune Pharmaceuticals Inc. (IPO)

March 24, 2000 to Present



Lambda Physik AG (IPO)

September 21, 2000 to Present



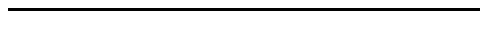
Luminex Corp. (IPO)

March 30, 2000 to Present



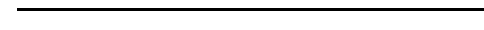
Nanogen Inc.

March 16, 2000 to Present



Oxford Asymmetry

March 29, 2000 to Present



Pharmagene (IPO)

July 31, 2000 to Present



Sequenom (IPO)

January 31, 2000 to Present



Genesis Research & Development (IPO)

September 22, 2000 to Present

