

## Public biotech 2008—the numbers

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The sour global economy has left many small public firms gasping for air.

*Nature Biotechnology's* survey of 399 public biotech companies confirms what many working in this industry already know: 2008, especially the second half, was a disastrous year, one in which the ever-present need for financing became the number one concern. However, despite a trickle of funds coming from public sources, R&D spending as well as revenues for the sector fared well in comparison to previous years. And for the second year in a row, the companies in our survey ended the year in the black (Box 1 and Fig. 1).

### Financing doldrums

Overall financing for the world's biotech sector fell 36% in 2008 from the amount raised the previous year, with the most notable drops coming in the public markets (follow-on financing, private investments in public equity (PIPEs), among others) and lesser declines seen from venture capital investment and in partnering funding (Fig. 2). Initial public offerings (IPOs) simply did not occur, follow-on offerings were rare and the total money raised in 2008 (\$33.8 billion) is the smallest amount raised since 2003.

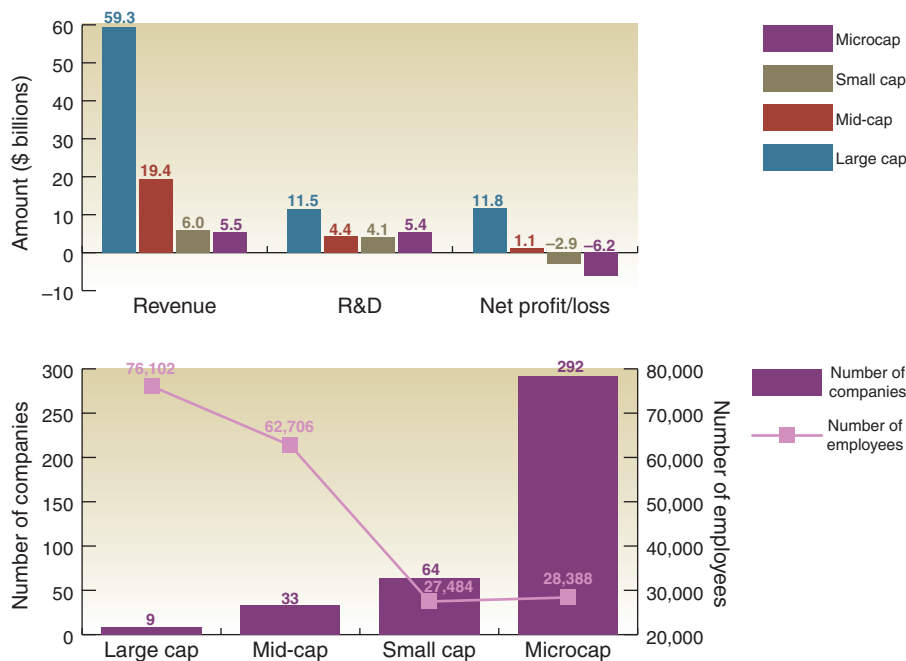
To get to the heart of the problem, *Nature Biotechnology* examined recent earnings reports (fourth quarter 2008 and first quarter 2009) and cash positions of public firms that most closely meet our definition of a biotech company (Box 1). The results point to where the trouble lies: whereas ~39% of public companies overall have less than one year's worth of cash, in the microcap sector

Data retrieval for this article was by Ernst & Young (Boston) and Riku Lähtenmäki, a freelance writer in Turku, Finland. Laura DeFrancesco, senior editor of *Nature Biotechnology*, provided the analysis. John Hodgson is editor-at-large and Brady Huggett business editor at *Nature Biotechnology*.

### Box 1 Source of the data

*Nature Biotechnology* has featured a survey of public biotech company financing since 1996. Over the years, we have refined our definition of what constitutes a biotech company. In general, we include companies whose primary commercial activity depends on the application of biological organisms, systems or processes, or on the provision of specialist services to facilitate the understanding thereof. We have purposefully excluded pharmaceutical companies, medical device companies and contract research organizations.

The company data were provided by Ernst & Young, as well as by individual company reports for companies listed on international stock markets. Top ten lists and any aggregate data are sourced appropriately, although most come from our analysis of data from BioCentury. In a few cases, year-end figures were not available so partial-year data were used and are so noted in a company-by-company data table (Table 9). Companies that were delisted from the major stock exchanges were excluded.



**Figure 1** Public biotech company revenue, R&D spending, profits and number of employees by market cap. Microcap, <\$250 million; small cap, \$250 million to <\$1 billion; mid-cap, \$1 billion to <\$5 billion; large cap, ≥\$5 billion.

(those with a market capitalization <\$250 million), that figure rises to 50%.

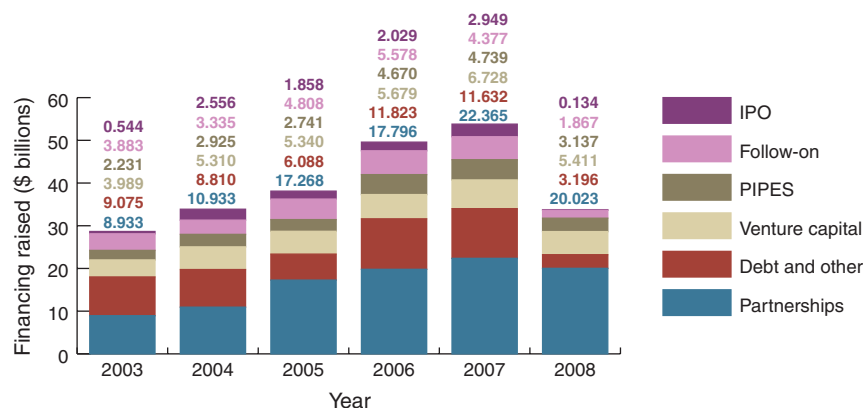
As most of the biotech sector falls into the microcap category, this means that the typical biotech firm in 2008 was most likely small, scrambling and nearly out of cash—even more so than usual. The cash crunch and rising bankruptcies have become the main topic of conversation for biotech, overshadowing any positive news.

However, the down economy appeared to matter little to biotech companies' investment in R&D. Research spending has increased by nearly \$3 billion annually in recent years, and jumped again last year, moving from \$22.8 billion in 2007 up to \$25.5 billion in 2008 (Fig. 1). The majority of that—\$11 billion—was put up by the large-cap firms, as they also record the highest revenues, but the 292 microcap biotech companies as defined by *Nature Biotechnology* contributed \$5.4 billion to the overall figure. Mid- and small-cap groupings invested about \$4.4 billion and \$4.1 billion, respectively.

And it is with some measure of pride that the biotech sector can say it was profitable in 2008, amidst the worst economic downturn seen in some time. Overall, global biotech turned in a profit of \$3.8 billion (Fig. 1), a marked increase over the barely \$1 billion in profit *Nature Biotechnology* reported for the sector in 2007. Here again, the heavy lifting was done by the large-cap firms, which boasted a profit of more than \$12 billion, an increase of more than \$1 billion from 2007. (As usual, the small and microcap firms ended the year in the red, with the microcaps recording a loss of almost \$6.2 billion.) Observers should note, though, that profitability of the sector as a whole is unlikely to happen again anytime soon, as Roche's (Basel) acquisition of Genentech (S. San Francisco, CA, USA) will erase Genentech's 2008 \$3.4 billion net income from the biotech landscape. That stream of revenue will not be easily replaced.

### Retreat by the public markets

If a good barometer for the health of the biotech industry is the IPO market, then 2008 was a spectacularly bad year for biotech (Fig. 3). Six IPOs occurred globally last year (in 2007, that number was 51); only one in the United States (Bioheart; Sunrise, FL, USA), which raised barely \$6 million (Table 1). And of the six, only one raised a notable amount of cash: MolMed (Milan), bringing in some \$85 million for its work in cancer. Both Bioheart and MolMed lost substantial market cap between their listings and the year's end, with Bioheart transferring its listing to the lower tier NASDAQ Capital Market



**Figure 2** Global biotech industry financing. Biotech funding dropped by 36% to \$34 billion in 2008 from \$53 billion in 2007. Partnership figures from Burrill & Co. are for deals involving a US company. BioCentury makes updates to its financing data on an ongoing basis. Sources: BCIQ; BioCentury Online Intelligence, Burrill & Co.

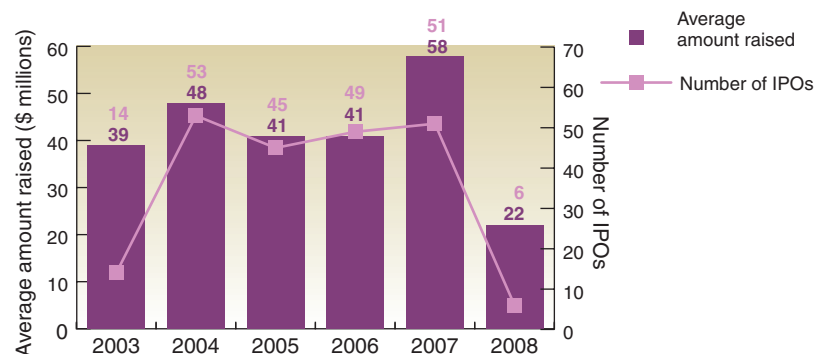
from the NASDAQ Global Market in June 2008 after receiving a noncompliance notice in May 2008. MolMed lost 50% of its market valuation by the end of 2008, but this then rose back to its opening level after the presentation of data from four clinical trials of its vascular targeting agent Arenegyr (NGR-hTNF; a recombinant fusion protein comprising CD13 ligand (C-NGR-CG peptide) and human tumor necrosis factor alpha), at the American Society for Clinical Oncology meeting in Orlando, Florida, at the beginning of June.

In 2007, a biotech IPO could be expected to bring in \$58 million—the highest average amount in the past six years. In 2008, the average IPO was \$22 million—the lowest over that same time frame (Fig. 3). The general distress of the public market, and the fact that several of the six IPOs took place on relatively junior stock exchanges (Alternext Paris, Sydney, Oslo Access, Milan) contributed to a devaluation of IPOs.

Debt funding also fell dramatically, from \$11.6 billion in 2007 to about \$3.2 billion

last year, with Biogen Idec (Cambridge, MA, USA) raising a third of that through a \$1 billion senior note deal, which gives the holders certain preferences in the event of financial distress or liquidation (Table 2). The follow-on public market wasn't much better, though established companies or those chugging toward a value-inflection point were able to raise money (Table 3). Acorda Therapeutics (Hawthorne, NY, USA), for instance, took advantage of investor interest in its sustained-release formulation of fampridine (4-aminopyridine), designed to improve walking in patients with multiple sclerosis, to raise \$131 million. The US Food and Drug Administration accepted Acorda's new drug application for the product in early May.

Service provider and sequencing giant Illumina (San Diego) raised the most money through a follow-on offering, bringing in more than \$352 million. But the company is profitable and has a diverse range of income streams: in fiscal year 2008, Illumina had revenue of \$573.2 million and a net profit of \$50.5 million. The fourth quarter of 2008



**Figure 3** Global biotech initial public offerings. IPOs were way down in 2008, both in numbers and amounts of money raised.



**Table 1 Initial public offerings of 2008**

Company	Date completed	Amount raised (\$ millions)	Underwriters	Development status <sup>a</sup>	Business category	Location
MolMed	2/29	85	Banca IMI, Societe Generale	Phase 3	Cancer	Milan
Ipsogen	6/10	19	Bryan, Garnier & Co.	Market (diagnostic)	Diagnostic	Marseille, France
PCI Biotech	6/10	12	Fondsfinans	Preclinical	Drug delivery	Oslo
Fluorotechnics	10/24	7	BBI	Market (tools & services)	Supply/service	Sydney, Australia
Bioheart	2/19	6	Dawson James Securities	Phase 2	Cardiovascular, gene/cell therapy	Sunrise, FL, USA
Genera Biosystems	5/21	5	Domain Capital	Development (diagnostic), Pivotal (device)	Diagnostic, pharmacogenetics	Victoria, Australia

Data are matched to the definition of biotech in **Box 1**. Source: BCIQ: BioCentury Online Intelligence

<sup>a</sup>Status at time of IPO

**Table 2 Top ten debt financings of 2008**

Company	Date completed	Amount (\$ millions)
Biogen Idec	2/29	1,000
Vertex Pharmaceuticals	2/13	288
OSI Pharmaceuticals	1/4	175
Therevance	1/17	173
Array BioPharma	12/23	80
InSite Vision	2/25	60
Cell Therapeutics	3/4	52
Ista Pharmaceuticals	9/26	40
Poniard Pharmaceuticals	10/6	28
Cell Therapeutics	6/12	23

Data are matched to the definition of biotech in **Box 1**. Source: BCIQ: BioCentury Online Intelligence

**Table 3 Top ten follow-on offerings of 2008**

Company	Date completed	Amount raised (\$ millions)
Illumina	8/7	352
Vertex Pharmaceuticals	9/18	220
Rigel Pharmaceuticals	1/31	135
Acorda Therapeutics	8/7	131
Vertex Pharmaceuticals	2/13	118
Incyte	7/31	109
Seattle Genetics	1/18	103
Sequenom	6/26	98
Acambis	5/20	85
Orexigen Therapeutics	1/24	81

Source: BCIQ: BioCentury Online Intelligence

was the company's thirtieth consecutive quarter of revenue growth.

One other stand-out exception was the completion of an \$85 million follow-on offering from Acambis, of Cambridge, UK—the offering notable not for its magnitude but for the rarity with which European companies are able to return to the market. In Acambis' case, the offer followed the award of a \$425 million biodefense contract from the US Centers for Disease Control and Prevention (Atlanta) and led to the acquisition of the company by Sanofi Aventis (Paris) in September 2008.

Smaller firms, years away from profitability, were of little interest to the public markets, and in general follow-on offerings were few and far between. Overall public funding in secondary offerings fell by more than 57% to \$1.87 billion last year. This is particularly troubling for biotech, as follow-on offerings are the first place companies turn when they need funding. When this dries up, an industry known for its lack of revenues and long product-development timelines begins a slow slide toward bankruptcy.

**Conserving cash**

Faced with dwindling cash supplies, firms have set about tightening their belts. The Biotechnology Industry Organization (BIO, Washington, DC, USA) reports that over the course of 2008, biotechs (public and private) in the United States collectively laid off more than 10,000 employees. Last year, 114 public companies announced they were restructuring their staff—code for employee layoffs. That's twice the number that laid off employees in 2007, and more than three times the number in 2006. The pace in 2009 has not slowed, with 52 companies announcing restructurings in the first quarter.

Along with layoffs comes the discontinuation of research. From September 2008 through May this year, more than 35 companies shelved clinical programs across a range of diseases, according to BIO, although the 399 companies *Nature Biotechnology* surveyed increased their R&D spending in 2008 over the previous year by about \$2.6 billion—an increase comparable to that seen in previous years.

The composite NASDAQ Biotech Index initially rose in 2008 from 835 on January 2 to 930 in mid-August but then plunged more than 200 points by the end of 2008, a 12.7% fall over the course of the year. As might be expected, this is very much in line with the fall in the market cap of the US companies surveyed here: however, the market cap of all the firms surveyed shows a 20% fall over the year. The collective market cap of the Australian companies fell 47%; German and French companies fell by a quarter; Danish firms by 44%; and companies in the UK by 56%. In some instances, the market cap drops could be attributed to the closure or takeover of individual firms.

Despite a general downturn in the market, the market cap of many public biotech companies grew in 2008. San Diego, USA-based Sequenom's stock price and valuation increased over 3.5-fold during the year (although it plummeted down at the end of April 2009 following a cost-cutting announcement and a pessimistic projection on sales in its genetic analysis business). Micromet (Munich), which now quotes on NASDAQ, saw its market cap triple. Large-cap companies like Amgen and Vertex increased nearly 30% in market valuation whereas Cubist and Cephalon added nearly 25% to their market caps, and Genentech 12%. Indeed, of 367 companies in this survey where year-end data were available for both 2007 and 2008, 72 (20%) increased market cap.

The average market cap drop for individual firms across the surveyed group was just under 25% during 2008. The number was the same for US companies, but lower for those in Belgium (22.6%), France (22.6%), Germany (20.2%), Sweden (20%) and Canada (17.2%). It was considerably higher for those in the UK (42.5%) and Denmark (59.2%) where over half the firms surveyed lost more than 50% of their value.

In the United States, decreasing market caps forced many small firms into violating listing regulations. Some 11 companies were delisted from NASDAQ in 2008, for regulatory issues or noncompliance (Table 4); another 8 have fallen afoul of regulations in the first four months of 2009. And for those firms unable to



raise money, cut spending or conserve enough cash, the end awaits: there were eight biotech bankruptcies last year—public and private.

The valuation squeeze had not, by the end of 2008, made an enormous impact on the level of employment in the public companies. Overall, there was barely a change among the surveyed companies, except in the UK, where there was a 14% decrease, and in Belgium, where there was a 20% decrease. These changes can be attributed both to mergers and acquisitions—BTG's (London) acquisition of Protherics (Cheshire, UK) and Solvay's (Weesp, The Netherlands) purchase of Innogenetics (Belgium), for instance.

When employment trends are examined within individual companies so that companies no longer in the survey are discounted, more than half of firms increased their head counts during 2008. On average, firms increased the number of employees by 9%. The biotech industry was still growing despite a funding crisis and valuation hits.

### Exploring all options

But if misfortune is opportunity seen from another angle, the cash crunch has opened doors for pharmaceutical firms. Staring at a 'patent expiration cliff' that seems to reach across most of the sector, and with a paucity of innovation in its collective pipeline, the pharma industry went on a buying spree in 2008 (Table 5). Two biotech stalwarts swallowed by pharma were Millennium Pharmaceuticals (Cambridge, MA, USA) and ImClone Systems (New York). Takeda (Osaka, Japan) paid more than a 50% premium for Millennium, acquiring its proteasome inhibitor Velcade (bortezomib) for multiple myeloma, and its oncology and inflammation research. Eli Lilly (Indianapolis) paid a 51% premium for ImClone, to snap up the Erbitux franchise (cetuximab for metastatic colorectal carcinoma and advanced squamous cell carcinoma of the head and neck), as well as the company's oncology pipeline, which includes several drugs in various stages of development.

Diversity in the vaccines sectors was reduced when Intercell (Vienna) bought Iomai (Gaithersburg, MD, USA) and when Sanofi Aventis bought Acambis (Cambridge, UK). Iomai's phase 3 travelers' diarrhea vaccine patch complemented Intercell's Japanese encephalitis vaccine product and also brought in an earlier-stage patch vaccine for pandemic influenza. Sanofi Aventis paid a 65% premium above Acambis' share price but the French pharma giant had clearly done its sums: the offer price of \$527.8 million was only just above the value of the \$425 million

**Table 4 Casualties in 2008**

Company	Status change	Date completed
<b>United States</b>		
Accentia Biopharmaceuticals	Bankruptcy	11/10
AlfaCell Pharmaceuticals	Delisted	8/1
Applied Biosystems	Merged with Invitrogen (now Life Technologies)	6/12
AtheroGenics	Delisted	10/10
Avant Immunotherapeutics	Merged with CellDex Therapeutics	2/27
CollaGenex Pharmaceuticals	Merged with Galderma	2/26
Cytogen	Acquired by EUSA Pharma	3/11
Favrille	Bankruptcy	7/7
Genitope	Delisted	5/28
Genelabs	Acquired by GSK	10/31
ImaRx Therapeutics	Delisted	10/17
ImClone Systems	Acquired by Lilly	11/24
Immunicon	Acquired by Veridex	8/1
Introgen Pharmaceuticals	Delisted	12/8
Invitrogen	Merged with Applied Biosystems	6/12
Iomai	Acquired by Intercell	5/12
Kosan Biosciences	Acquired by Bristol-Myers Squibb	5/29
LifeCell	Delisted	5/28
Lipid Sciences	Delisted	10/1
Memory	Acquired by Roche	11/25
Millennium Pharmaceuticals	Acquired by Takeda	4/10
Omrix	Acquired by Johnson & Johnson	11/24
Renovis	Merged with Evotec	5/1
SGX Pharmaceuticals	Acquired by Lilly	7/8
Sirtris Pharmaceuticals	Acquired by GSK	4/23
Tercica	Acquired by Ibsen	6/5
Third Wave Technologies	Acquired by Hologic	6/9
Vermillion Pharmaceuticals	Delisted	11/30
<b>Outside United States</b>		
Bellus Health Pharmaceuticals	Delisted	12/29
Innogenetics	Acquired by Solvay	9/9
Jerini	Acquired by Shire	7/4
Acambis	Acquired by Sanofi Pasteur	7/25
GeneMedix	Changed name to Reliance GeneMedix	10/16
Protherics	Acquired by BTG	12/4

Data are matched to the definition of biotech in **Box 1**. Source: BCIQ: BioCentury Online Intelligence

**Table 5 Top ten announced mergers and acquisitions 2008**

Target	Acquirer	Month completed	Deal value (\$ millions) <sup>a</sup>
Millennium	Takeda	May	8,200.0
Applied Biosystems	Invitrogen	December	6,700.0
ImClone	Lilly	November	6,500.0
Ventana	Roche	February	3,400.0
LifeCell	Kinetic Concepts	June	1,700.0
Sirtris	GSK	June	720.0
Third Wave Technologies	Hologic	July	580.0
Acambis	Sanofi Pasteur	September	525.3
Jerini	Shire	December	516.6
Omrix	Johnson & Johnson	December	438.0

<sup>a</sup>Value of deal on completion. Source: BCIQ: BioCentury Online Intelligence

**Table 6 Top ten research partnership and licensing deals of 2008**

Researcher	Investor	Date announced	Deal value (\$ millions)	Details
Actelion	GSK	7/14	3,200	Exclusive co-development and co-marketing rights to Almorexant, an orexin receptor antagonist, currently in phase 3
Isis Pharmaceuticals	Genzyme	1/10	1,900	Mipomersen, Isis' antisense-based, lipid-lowering treatment, in phase 3
Acceleron	Celgene	2/20	1,900	Jointly develop and commercialize ACE-011 to treat cancer; option to jointly develop three undisclosed discovery programs for cancer and cancer-related bone loss
Osiris Therapeutics	Genzyme	11/4	1,400	Commercialization of two adult stem cell products (Prochymal and Chondrogen)
PDL Pharmaceuticals	Bristol-Myers Squibb	8/21	1,200	Elotuzumab, an anti-CS1 antibody, currently in phase I clinical trials in multiple myeloma; option on PDL241, another anti-CS1 antibody (preclinical)
Amgen	Takeda	2/4	1,200	(i) Vectibix and up to 12 molecules from Amgen's clinical pipeline (early- to mid-stage) over various therapeutic areas; (ii) covers Amgen's phase 2 cancer-drug candidate motesanib
Alnylam Pharmaceuticals	Takeda	5/27	>1,000	RNAi therapeutics for oncology and metabolic disease
Exelixis	Bristol-Myers Squibb	12/12	1,000	Development of two cancer drugs, one in phase 3 (small-molecule inhibitor of MET, VEGFR2 and RET) and a small-molecule inhibitor of RAF in phase 1
Thrombogenics	Roche	6/18	774	Develop phase 1b antibody for cancer
Addex Pharmaceuticals	Merck	1/3	702	Develop and market schizophrenia drug
Immunomedics	Nycomed	7/14	620	Co-develop and market anti-CD-20 antibody (veltuzumab) for non-cancer indications (phase 2)
Regulus	GSK	4/17	598	Four microRNA antagonists for inflammatory diseases

Data are matched to the definition of biotech in **Box 1**. Source: BCIQ: BioCentury Online Intelligence, Burrill & Company, Recombinant Capital.

contract award to Acambis by the US government in April 2008, plus the \$85 million raised in a follow-on offer in May 2008.

But pharma was also buying smaller firms such as Sirtris (Cambridge, MA, USA), a young startup notable for being a front-runner in researching sirtuins, a class of enzymes believed to be involved in aging. GlaxoSmithKline (GSK; London) paid an 84% premium in their quest for Sirtris, hoping to apply its drug discovery technology to sirtuin modulation and bolster GSK's metabolic, neurology, immunology and inflammation research. Sirtris also brings its research on SIRT1 activators for type 2 diabetes.

Some small biotechs had sunk to such

depths that pharma was able to pay eye-popping premiums and still acquire the company on the cheap. GSK purchased the infectious disease company GeneLabs Technologies (Redwood City, CA, USA) for \$57 million at \$1.30 a share—a 465% premium to its beaten-down trading price.

For those companies neither attractive enough to catch pharma's eye, nor sure-footed enough to secure further funding from today's discerning financiers, all options come into play, including selling off assets and calling it quits. The Cytogen-EUSA Pharma merger is just such an example. Cytogen (Princeton, NJ, USA) announced in late November 2007 that it was reviewing

strategic alternatives, including securing more financing, finding a licensing agreement, selling either assets or the whole company. It eventually settled on specialty pharma EUSA (headquartered in Oxford, UK), which paid 62 cents per share in cash, a premium of about 35% over Cytogen's trading price before the announcement was made. With its focus on oncology, pain control and critical care, EUSA may have been attracted to Cytogen's imaging agent for prostate cancer (Prostascint, capromab pendetide) or Caphosol, an advanced electrolyte solution approved in the United States for oral mucositis and dry mouth. EUSA launched the drug early this year in Europe.

**Table 7 Top ten biotech drugs of 2008**

Trade (generic)/drug maker	Indication	2008 revenues (\$ millions)	2007 revenues (\$ millions) <sup>a</sup>
Enbrel (etanercept)/Amgen	Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, plaque psoriasis, juvenile rheumatoid arthritis	6,191	5,273
Rituxan (rituximab)/Genentech, Biogen Idec	Non-Hodgkin's lymphoma, rheumatoid arthritis	5,480	4,604
Remicade (infliximab)/Johnson & Johnson	Crohn's disease, ankylosing spondylitis, psoriatic arthritis, ulcerative colitis, rheumatoid arthritis, psoriasis	5,273	4,420
Avastin (bevacizumab)/Genentech	Colorectal cancer, non-small-cell lung cancer, breast cancer, brain cancer (approved May 2009)	4,807	3,431
Humira (adalimumab)/Abbott	Rheumatoid arthritis, psoriatic arthritis, psoriasis, Crohn's disease, ankylosing spondylitis, juvenile rheumatoid arthritis	4,521	3,064
Gleevec/Glivec (imatinib mesylate)/Novartis	Chronic myelogenous leukemia, gastro-intestinal stromal tumors, acute lymphocytic leukemia, hypereosinophilic syndrome, mastocytosis, dermatofibrosarcoma protuberans, myelodysplastic syndrome, myeloproliferative disorders	3,700	3,050
Lantus (insulin glargine (rDNA origin) injection)/Sanofi Aventis	Types I and II diabetes	3,668	2,840
Neulasta (pegfilgrastim)/Amgen	Infection associated with chemotherapy-induced neutropenia	3,318	3,000
Aranesp (darbepoetin alfa)/Amgen	Anemia	3,137	3,614 <sup>a</sup>
Prevnar pneumococcal 7-valent conjugate vaccine/Wyeth	Prevention of diseases caused by <i>Streptococcus pneumoniae</i>	2,716	2,439

<sup>a</sup>Aranesp, in fourth place in terms of revenue in 2007, fell to ninth place in 2008. Source: BioMed Tracker



Of particular note is the acquisition of Genentech by Roche. Though this did not close in 2008, the original bid for the firm surfaced last year. Perhaps more than any other acquisition of late, this one typifies the trend swirling through the industry: pharma is looking to lock up the large profits and long market-lives of biologics, hoping to bring innovation to its own pipelines of small molecules, now endangered by generics. Roche, a long-time majority holder of Genentech stock, had left the biotech alone to run its business. But in 2008 Roche decided it wanted more control, partially because its option to take non-US rights to any drug coming out of Genentech's pipeline was due for renegotiation in 2015.

Although there was much initial wrangling over price, the merger closed before the end of March this year, bringing one of the biggest success stories in biotech under Roche's wing. At a stroke, the disappearance of Genentech into pharmaceutical full ownership will remove around 20% of the US public biotech market capitalization and shift around 8% of the public biotech sector's employees into the pharmaceutical industry.

### Desperately seeking partners

Pharma's need for products is also a driving force behind licensing deals. Whereas overall funding for biotechs fell dramatically in 2008, the money received from partnerships declined by proportionately less, by \$2 billion, to about \$20 billion. This means that partnering money exceeded the funds raised from all other sources combined, increasing as a percentage of biotech funding, from 42% in 2007 to 59% last year (Fig. 1).

GSK placed three partnerships in our top ten research deals of 2008; it would pay out a combined \$5.6 billion in those deals if all milestones are hit (Table 6). But of particular interest last year was the deal between Genzyme (Cambridge, MA, USA) and Isis (Carlsbad, CA, USA), over mipomersen, an apo-B synthesis inhibitor based on Isis' antisense technology. The drug, designed to treat familial hypercholesterolemia, was shopped to as many as ten interested parties, yet it was the biotech Genzyme that won the day, having convinced Isis it could successfully market the drug if approved, because of Genzyme's own history of selling niche drugs.

Genzyme also invested in stem cell products last year, signing Osiris (Columbia, MD, USA) to a deal valued at up to \$1.25 billion, with \$125 million upfront, for the commercialization of two late-stage mesenchymal stem cell products, prochymal (for treating graft

**Table 8 Top ten revenue gainers and losers in 2008**

	Absolute change in revenue (\$ millions)	2008 revenue (\$ millions)	Percent change since 2007
<b>Gainers</b>			
Monsanto	3,016	11,365.0	36
Genentech	1,694	13,418.0	14
Gilead Sciences	1,106	5,335.8	26
Biogen Idec	926	4,097.5	29
Celgene	849	2,254.8	60
Genzyme	792	4,605.0	21
Life Technologies	339	1,620.3	26
Bio-Rad Laboratories	303	1,764.4	21
Myriad Genetics	254	386.6	192
Qiagen	243	893.0	37
<b>Losers</b>			
Proton Therapeutics	-192.0	578.1	-25
Nektar Therapeutics	-183.0	90.2	-67
XenoPort	-72.0	42.0	-63
Replidyne	-59.0	0.0	-100
Idenix Pharmaceuticals	-58.0	10.0	-85
Nuvelo	-32.0	15.3	-67
Incyte	-31.0	3.9	-89
Trimeris	-29.0	20.6	-58
Altus Pharmaceuticals	-26.0	2.2	-92
Anadys Pharmaceuticals	-24.0	0.0	-100

versus host disease) and chondrogen (for repairing torn or injured menisci).

Whereas the two biggest deals of the year were for phase 3 drugs—Genzyme/Isis and GSK/Actelion for Almorexant, a first-in-class orexin receptor antagonist for insomnia—there were plenty of sizable agreements for earlier-stage products. PDL (Fremont, CA, USA) and Bristol-Myers Squibb (New York) entered into a partnership for a drug in phase 1, elotuzumab, an antibody that binds to the cell surface glycoprotein 1 of multiple myeloma.

Some deals had no clinical product involvement at all, such as Takeda's potentially \$1 billion deal with Alnylam (Cambridge, MA, USA), which focuses on RNA interference (RNAi) drugs in oncology and metabolic disease. Rounding out its busy year, Takeda also signed a partnership with Amgen (Thousand Oaks, CA, USA) for a host of products across a range of disease areas.

### Product sales climb

Biotechs might be struggling with investor perceptions, but their products remain hot property. In general, biologics have grown in sales incrementally year on year, which also proved true in 2008 (Table 7). Topping last year's list of revenue producers is Amgen's tumor necrosis factor inhibitor Enbrel (etanercept), approved for arthritis and four other inflammatory diseases, with worldwide rev-

enue of nearly \$6.2 billion. Also notable is Abbott's (Abbott Park, IL, USA) Humira (adalimumab), which recorded global revenue of \$4.5 billion—a whopping 47.6% increase over 2007. The drug was initially approved in 2002 for rheumatoid arthritis, and Abbott has consistently increased its usage. It is now approved in six indications, having been cleared last year for moderate to severe polyarticular juvenile idiopathic arthritis in patients age 4 and older, as well as for psoriasis.

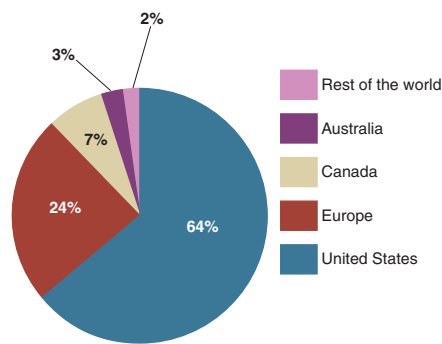
Avastin (bevacizumab), Genentech's monoclonal antibody that binds to the vascular endothelial growth factor protein, continued its growth, with international revenue increasing from \$3.4 billion in 2007 to \$4.8 billion last year. It was approved for breast cancer in 2008, and for brain cancer in May, but it lost a potentially lucrative market, when it failed in trials of early-stage colon cancer in 2009.

Many companies increased sales impressively during 2008 (Table 8). Genentech sales were up nearly \$4 billion (42% over 2007); Monsanto (St. Louis) sales increased \$3.4 billion (40% up); Gilead (Foster City, CA, USA), Biogen Idec (Cambridge, MA, USA), Celgene (Summit, NJ, USA) and Genzyme (Cambridge, MA, USA) sales were up \$0.8–1.1 billion. Sales for supplier companies like Illumina and Qiagen

(Venlo, The Netherlands) increased by over \$200 million each (up 56% and 37%, respectively) whereas diagnostics company Myriad Genomics (Salt Lake City, UT, USA) increased sales 146% over the year from \$157 million to \$386 million. Approximately 200 of the companies surveyed increased sales in 2008, whereas around 130 lost ground. Sales losses were generally smaller than sales gains with Nektar Therapeutics (San Carlos, CA, USA; \$183 million, down 67%), the French company BioMerieux (\$176 million, down 10%), and Xenoport (Santa Clara, CA, USA; \$72 million, down 63%) losing the most.

A former trailblazing class of biologic also saw its revenues stagnate. Aranesp (darbepoetin alfa), one of several erythropoiesis-stimulating agents, contracted, falling to \$3.1 billion from \$3.6 billion in 2007. Amgen attributed the flagging sales in part to a decline in demand because of regulatory changes (new black box warning on labels of these agents) and new recommendations on coverage from the Center for Medicare and Medicaid Services (Baltimore), both enacted in 2007. There were additional product label changes in the third quarter of 2008.

Looking forward, the fear is that the financing drought is increasing the chances that a future biologic blockbuster like Enbrel (or indeed Aranesp) is sitting on a shelf. BIO reports that from September 2008 to May 2009, more than 35 companies in the United States suspended development programs that had turned out positive clinical data in several areas with unmet therapeutic needs.



**Figure 4** Public biotech companies by geographical location. Source: Company reports, *Nature Biotechnology*

### The outlook

In past years, the question for biotech has been about profitability: when will this industry finally move collectively into the black? For now, that has taken a back seat to the question of survival. Business consultant Ernst & Young (New York) charts the number of firms that are operating with less than 12 months' worth of cash, and it typically finds that 20–25% of public companies are caught in that particular predicament. Though the companies on the list change from one year to the next, the percentage remains the same, which means some find their way out even as others fall in. They do not all go bankrupt. Nearly double that number finds itself in trouble today, which means that the industry is mired in something deeper. If past history is any indication, they will not all go under. But, it's hard to predict what the landscape will look like one year from now.

One of the keenest indicators of fiscal tightening is R&D spending. Although R&D is, in essence, the future life blood of most biotech companies, cutting research spending is nevertheless among the first rationalizations that companies will make in times of stress. In fiscal 2007, two-and-a-half times as many companies increased R&D spending as decreased it—246 to 94 (Table 9). In 2008, there was near equality with 151 companies cutting this investment in the future while 168 increased the R&D cash burn rate. Although cutting \$236 million from its roughly \$3 billion R&D budget may not harm a company like Amgen unduly, the same could not be said for firms lower down the food chain. Cutting out the value-creating part of the company is probably not the best way to conserve value for the future, albeit that other options might be limited.

It might be instructive to look at what is happening today in the United States, which still leads the world in numbers of biotech companies (Fig. 4). According to BIO, 16% of US public biotech companies that were active at the beginning of 2008 ended the year either in bankruptcy, restructuring or suspended operations (9%), or were acquired (7%). That represents a significant contraction.

By early May, three more firms had filed for bankruptcy. At the time of writing, the NASDAQ market is in positive territory for 2009—impressive considering the massive bloodletting it provided last year—but until the financing markets open back up, biotech can expect more of the same. Batten down the hatches. 2009 will likely look worse than 2008. **15**

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Company Name	Ticker	Market cap (\$ M) <sup>a</sup>	Number of employees	Sales		R&D		Net Inc		Company Name	Ticker	Market cap (\$ M) <sup>a</sup>	Number of employees	Sales		R&D		Net Inc	
				(\$ M)	% change	(\$ M)	% change	(\$ M)	% change					(\$ M)	% change	(\$ M)	% change	(\$ M)	% change
3SBio	SSRX	148	483	35.5	35%	3.3	93%	5.8	-51%	Amylin Pharmaceuticals	AMLN	1,493	1,800	840.1	8%	293.1	6%	-315.4	-49%
AP Pharma	APPA	13	32	0.4	-10%	19.5	1%	-23.1	-15%	Anadys Pharmaceuticals	ANDS	45	50	0.0	-100%	26.0	-9%	-32.4	-253%
Astrom Biosciences	ASTM	67	45	0.4	-51%	13.0	28%	-17.9	-5%	Anesiva	ANSV	14	78	0.3	496%	36.2	56%	-103.2	-74%
Ablynx	ABLX	222	205	20.6	77%	39.5	59%	-20.1	-22%	Anika Therapeutics	ANIK	35	84	35.8	16%	7.4	70%	3.6	-40%
ACADIA Pharmaceuticals	ACAD	33	63	1.6	-79%	56.8	-2%	-64.2	-14%	Antares Pharma	AIS	25	24	5.7	-28%	8.0	43%	-12.7	-48%
Accelrys	ACCL	118	364	81.4	3%	16.2	-6%	1.8	133%	Antigenics	AGEN	32	80	2.7	-52%	21.8	-5%	-28.7	22%
Access Pharmaceuticals	ACCP	6	9	0.3	411%	3.7	44%	-17.2	21%	Antisense Therapeutics	ANP	16	5	4.9	1302%	3.7	52%	-1.5	56%
Achillion Pharmaceuticals	ACHN	18	54	-0.2	-106%	21.2	-25%	-28.2	0%	Antisoma	ASM	254	71	57.9	397%	27.0	27%	18.1	226%
Acorda Therapeutics	ACOR	774	174	47.8	21%	36.6	63%	-74.3	-96%	Aqua Bounty	ABTX	3	0	0.1	-65%	2.3	-6%	-6.7	3%
Acrux	ACR	75	43	5.1	38%	NA	NA	-3.6	36%	Aradigm	ARDM	14	38	0.3	-74%	16.5	-2%	-22.6	7%
Actelion	ATLN	5,714	2,054	1,295.2	12%	329.2	28%	282.6	158%	Arena Pharmaceuticals	ARNA	309	499	9.8	-49%	204.4	37%	-237.6	-66%
Active Biotech	ACTI	354	90	6.6	343%	25.5	9%	-22.3	13%	Ariad Pharmaceuticals	ARIA	59	150	7.1	98%	50.8	28%	-71.1	-21%
Acusphere	ACUS	3	118	2.7	1%	34.5	-20%	-67.7	-26%	ArQule	ARQL	186	108	14.1	54%	49.6	-8%	-50.9	5%
Addex Pharmaceuticals	ADXN	196	135	23.6	5405%	38.8	61%	-19.4	37%	Array BioPharma	ARRY	193	358	27.2	-33%	100.4	132%	-128.4	-183%
Adherex Technologies	ADH	5	18	NA	NA	NA	NA	NA	NA	Arthro Kinetics	AKI	20	35	NA	NA	NA	NA	NA	NA
Adolor	ADLR	77	129	49.5	442%	52.7	27%	-30.1	38%	Artimplant	ARTI	21	25	1.5	-26%	1.9	5%	-2.8	-68%
Advanced Life Sciences Holdings	ADLS	15	30	0.2	NA	15.7	-39%	-22.8	29%	Autolmmune	AIMM	18	1	0.3	7%	0.2	21%	-0.3	-192%
AETerna Zentaris	AEZS	25	109	38.5	-9%	57.1	-100%	-56.1	98%	Auxilium Pharmaceuticals	AUXL	1,202	380	125.4	31%	54.5	27%	-46.3	-14%
Affymax	AFFY	153	147	82.9	87%	137.5	98%	-86.5	-101%	Avalon Pharmaceuticals	AVRX	6	36	0.3	-62%	15.5	1%	-21.8	-1%
Affymetrix	AFFX	210	1,128	410.2	10%	84.5	16%	-307.9	-2,545%	AVANIR Pharmaceuticals	AVNR	32	20	6.6	-28%	16.6	-48%	-17.2	74%
Albany Molecular Research	AMRI	307	1,357	229.3	19%	13.1	2%	20.6	130%	AVI BioPharma	AVII	47	83	21.3	94%	29.0	-17%	-24.0	12%
Alchemia	ACL	37	47	0.0	-99%	2.3	-44%	-7.9	15%	Avigen	AVGN	23	12	7.1	NA	23.6	14%	-25.1	0%
Alexion Pharmaceuticals	ALXN	2820	504	259.1	260%	62.6	-9%	33.1	136%	Axis-Shield	ASD	210	519	125.0	28%	20.1	75%	6.6	125%
Alexza Pharmaceuticals	ALXA	104	111	0.5	NA	61.6	35%	-58.5	-30%	Basilea Pharmaceutica	BSLN	674	300	10.5	46%	85.6	-16%	-126.2	-13%
Algeta	ALGETA	116	34	0.0	NA	NA	NA	-26.4	-125%	Biocon	BO	583	2,772	167.2	1%	3.8	20%	39.3	23%
Alkermes	ALKS	1015	570	345.4	42%	98.6	-20%	125.8	-33%	BioCryst Pharmaceuticals	BCRX	52	80	56.6	-21%	73.3	-22%	-24.7	15%
Allergy Therapeutics	AGY	15	362	45.5	21%	23.9	-36%	-29.8	13%	Biodel	BIOD	114	60	0.0	NA	33.0	333%	-42.4	-300%
Alliance Pharmaceutical	ALLP	0	2	0.0	-38%	0.2	-92%	-1.6	85%	Biofrontera	BBF	52	28	0.5	153%	8.4	85%	-20.0	-88%
Allion Healthcare	ALLI	107	271	340.7	38%	0.0	NA	7.5	131%	BioGen Idec	BIIB	13896	4,700	4097.5	29%	1072.1	16%	783.2	23%
Allos Therapeutics	ALTH	497	81	0.0	NA	23.8	37%	-51.7	-31%	Bioheart	BHRT	16	24	0.2	-51%	6.2	-45%	-14.2	21%
Alnylam Pharmaceuticals	ALNY	1024	173	96.2	89%	96.9	-20%	-26.2	69%	Bioinvent	BINV	141	108	31.0	76%	26.5	53%	2.0	201%
Alpha Innotech	APNO	8	53	17.6	15%	1.3	2%	0.1	110%	BioLineRx	BLRX	95	47	NA	NA	NA	NA	NA	NA
Alseres Pharmaceuticals	ALSE	26	27	0.0	NA	10.9	4%	-20.8	-7%	BioMarin Pharmaceutical	BMRN	1777	649	296.5	144%	93.3	19%	30.8	295%
Altus Pharmaceuticals	ALTU	16	38	2.2	-92%	83.6	18%	-96.6	-53%	Biomerieux	BIM	3,109	6,140	1,469.2	4%	175.6	1%	172.0	33%
AMAG Pharmaceuticals	AMAG	610	259	1.9	-24%	31.7	31%	-71.6	-111%	BioMimetic Therapeutics	BMTI	172	88	3.1	-55%	24.6	28%	-8.0	67%
Amarillo Biosciences	AMAR	2	6	0.1	57%	0.5	-1%	-1.9	23%	BioMS Medical	MS	260	2	52.6	NA	37.9	-4%	-0.4	99%
Amarin <sup>b</sup>	AMRN	35	25	0.0	NA	5.1	NA	-8.0	NA	Bioniche Life Sciences	BNC	25	198	32.0	14%	12.9	6%	-11.3	-698%
Ambriila Biopharma	AMB	3	14	3.6	9,983%	8.8	-15%	-32.4	-27%	Biopure	BPUR	5	6	3.7	46%	4.6	-30%	-16.8	52%
Amgen	AMGN	61,187	16,800	15,003.0	2%	3,030.0	-7%	4,196.0	33%	Bio-Rad Laboratories	BIO	2,055	6,600	1,764.4	21%	159.5	14%	89.5	-4%
Amicus Therapeutics	FOLD	180	115	15.0	739%	37.8	22%	-39.4	4%	BioSante Pharmaceuticals	BPAX	27	23	3.5	620%	15.9	230%	-17.4	-130%
Amsterdam Molecular Therapeutics	AMT	56	90	0.3	103%	17.4	34%	-22.4	-13%	Biota Holdings	BTA	188	34	28.3	-30%	7.4	25%	-4.7	-132%
										Biotage	BIOT	59	292	47.4	-3%	4.3	-3%	36.8	201%
										Biotest	BIO3	482	2,108	559.6	30%	57.8	27%	37.2	63%
										Biotie Therapies	BTH1V	50	42	6.8	-35%	11.5	-4%	-7.2	-217%
										Biovitrum	BVT	406	485	140.3	-9%	82.5	-3%	-41.2	-525%

(continued)

Table 9 List of public biotech companies (continued)

Company Name	Ticker	Market cap (\$ M) <sup>a</sup>	Number of employees	Sales		R&D		Net Inc		Company Name	Ticker	Market cap (\$ M) <sup>a</sup>	Number of employees	Sales		R&D		Net Inc	
				(\$ M)	% change	(\$ M)	% change	(\$ M)	% change					(\$ M)	% change	(\$ M)	% change	(\$ M)	% change
Bone Medical	BNE	13	1	0.0	-33%	1.3	-27%	-2.0	17%	DOV Pharmaceutical	DOVP	1	13	NA	NA	NA	NA	NA	NA
Caliper Life Sciences	CALP	47	489	134.1	-5%	19.9	-20%	-68.3	-184%	Direct	DRRX	278	130	27.1	-12%	39.4	3%	-43.9	-80%
Callisto Pharmaceuticals	CLSP	4	9	0.0	NA	5.4	-16%	-9.7	-22%	DUSA Pharmaceuticals	DUSA	25	86	29.5	7%	6.6	11%	-6.3	58%
Cangene	CNJ	335	700	179.5	78%	36.7	80%	39.2	202%	Dyax	DYAX	229	164	43.4	66%	68.1	6%	-66.5	-18%
Celera Group - Applera	CRA	896	626	175.2	249%	35.2	-43%	-124.6	-245%	Dynavax Technologies	DVAX	33	155	37.1	163%	44.8	-32%	-20.8	65%
Celgene	CELG	2,532.9	2,441	2,254.8	60%	931.2	133%	-1,533.7	-777%	Elan	ELN	2,810	1,687	1,000.2	32%	323.4	23%	-71.0	82%
Cell Genesys	CEGE	19	16	94.6	6,753%	92.5	-13%	-47.0	53%	Elite Pharmaceuticals	ELTP	2	16	2.1	198%	3.5	-39%	-7.3	27%
Cell Therapeutics	CTIC	18	194	11.4	8,902%	51.6	-28%	-180.0	-30%	Emergent Biosolutions	EBS	781	587	178.6	-2%	59.5	10%	20.7	-10%
Collectis	ALCLS	98	67	14.0	277%	NA	NA	0.2	104%	Emisphere Technologies	EMIS	24	20	0.3	-94%	12.8	-39%	-24.4	-44%
Cellegy Pharmaceuticals	CLGY	1	2	0.0	NA	0.0	-100%	-1.5	20%	Endo Pharmaceuticals Holdings	ENDP	3,474	1,216	1,260.5	16%	110.2	-20%	261.7	15%
CEL-SCI	CVM	34	30	0.0	-91%	4.4	40%	-7.8	25%	Entelos		1	37	NA	NA	NA	NA	NA	NA
Celsis	CEL	61	262	56.1	18%	0.6	32%	6.7	14%	EntreMed	ENMD	14	21	7.5	1%	20.1	-15%	-23.9	-6%
Cephalon	CEPH	5273	2,780	1,974.6	11%	362.2	-2%	222.5	215%	Enzo Biochem	ENZ	183	475	82.1	102%	8.7	-1%	-19.4	-38%
Cepheid	CPHD	598	547	169.6	31%	43.3	38%	-21.7	-1%	Enzon Pharmaceuticals	ENZN	262	351	196.9	6%	58.1	6%	-2.7	-103%
Cerep	CER	35	291	40.7	-2%	9.0	18%	2.5	-28%	Epigenomics	ECX	62	90	2.6	-17%	NA	NA	-18.1	6%
Cerus	CERS	23	107	16.5	49%	10.2	-32%	-29.2	36%	EpiStem Holdings	EHP	37	35	3.0	52%	3.8	20%	-1.7	-11%
CK Life Sciences	8222	422	1,315	385.9	43%	7.9	-32%	-45.5	-406%	EPIX Pharmaceuticals	EPIX	43	91	28.6	91%	46.2	-20%	-36.7	42%
Clavis Pharma	CLAVIS	19	21	0.1	-56%	7.3	29%	-12.6	-45%	e-Therapeutics	ETX	28	18	0.1	NA	NA	NA	-2.9	-71%
Cleveland BioLabs	CBLI	29	32	4.7	133%	13.2	-24%	-14.0	48%	Evolutec	EVC	NA	NA	NA	NA	NA	NA	NA	NA
Co.don	CNW	11	30	2.0	27%	NA	NA	NA	NA	Evotec	EVT	97	418	52.4	20%	56.3	15%	-103.6	-63%
Cobra Bio-Manufacturing	CBF	3	123	10.3	-24%	0.8	-12%	-4.8	-85%	EXACT Sciences	EXAS	16	4	-0.9	-148%	2.0	-58%	-9.7	19%
Columbia Laboratories	CBRX	68	62	36.3	23%	6.2	7%	-14.1	2%	Exelixis	EXEL	530	676	117.9	4%	257.4	14%	-162.9	-89%
CombinatoRx	CRXX	22	73	14.1	-5%	60.9	10%	-65.1	-22%	Exiqon	EXQ	79	211	22.8	159%	10.3	100%	-20.5	-70%
Commonwealth Biotechnologies	CBTE	2	65	9.4	5%	0.0	NA	-9.9	-258%	Flamel Technologies	FLML	143	302	38.6	5%	36.3	-17%	-12.1	68%
Compugen	CGEN	31	72	0.3	88%	9.3	-5%	-12.5	-9%	<b>Fluorotechnics</b>	FLS	11	13	NA	NA	NA	NA	NA	NA
Cortex Pharmaceuticals	COR	27	13	0.0	NA	10.8	16%	-14.6	-13%	Galapagos	GLPGA	194	482	101.8	17%	51.2	26%	-19.3	34%
CruCell	CRXL	1,389	1,126	353.4	31%	92.9	10%	19.3	134%	Genaera	GENR	6	16	1.5	-46%	11.7	-11%	-16.0	-2%
CryoLife	CRY	273	435	105.1	11%	5.3	19%	32.9	357%	Genentech	G6A	31	193	20.8	27%	2.6	81%	0.9	-43%
Cubist Pharmaceuticals	CBST	1,377	554	433.6	47%	126.7	49%	169.8	253%	Genentech	DNA	87,224	11,186	13,418.0	14%	2,800.0	14%	3,427.0	24%
CuraGen	CRGN	26	16	1.2	1,234%	15.1	-59%	24.8	-2%	<b>Genera Biosystems</b>	GBI	18	7	0.0	-14%	0.1	-79%	-2.3	-12%
Curalogic	CUR	NA	8	NA	NA	NA	NA	NA	NA	Generex Biotechnology	GNBT	38	27	1.0	280%	16.6	93%	-46.2	13%
Curasan	CUR	26	21	11.6	-10%	NA	NA	-1.2	37%	Genescan Europe	GEP1	36	69	22.2	16%	0.1	-42%	9.3	32%
Curis	CRIS	48	34	8.4	-49%	13.2	-11%	-12.1	-74%	Genetic Technologies	GENE	10	60	11.3	5%	0.9	2%	-3.9	-25%
CV Therapeutics	CVTX	565	550	154.5	87%	75.1	-21%	-98.5	46%	Genitex	GTX	55	181	38.4	14%	2.8	8%	2.9	-19%
Cyanotech	CYAN	8	53	13.9	31%	0.2	-7%	1.1	153%	Genfit	ALGFT	89	127	11.6	-8%	0.0	NA	-5.2	-41%
Cyclacel Pharmaceuticals	CYCC	9	51	0.9	580%	18.9	-4%	-40.4	-68%	Genmab	GEN	1790	555	132.6	41%	253.3	68%	-171.8	-152%
Cypress Bioscience	CYPB	259	145	17.2	23%	9.7	25%	-18.2	-623%	Genomic Health	GHDX	553	387	110.6	73%	28.6	30%	-16.1	41%
Cytokinetics	CYTK	141	110	12.4	-9%	54.0	1%	-56.4	-15%	Genoptix	GDXD	566	326	116.2	96%	1.2	121%	31.4	135%
Cytori Therapeutics	CYTX	106	85	6.9	13%	17.4	-13%	-30.0	-5%	genOway	ALGEN	12	58	8.9	40%	NA	NA	-1.6	-9%
Cytos Biotechnology	CYTN	52	133	17.3	-45%	34.7	-1%	-22.9	-278%	Gen-Probe	GPRO	2329	991	472.7	17%	103.6	4%	107.0	24%
CytRx	CYTR	28	33	6.3	-16%	10.5	-44%	-27.0	-24%	Genta	GNTA	NA	25	NA	NA	NA	NA	NA	NA
DARA BioSciences	DARA	15	5	0.0	NA	7.3	138%	-11.6	-657%	Gentium	GENT	10	74	10.1	2%	12.7	-34%	-26.3	44%
deCODE genetics	DCGN	17	331	58.1	44%	30.7	-43%	-81.0	15%	GenVec	GNVC	38	98	15.1	8%	33.8	30%	-26.1	-39%
Dendreon	DNDN	444	198	0.1	-85%	50.1	-35%	-71.6	28%	Genzyme	GENZ	17,954	11,000	4,605.0	21%	1,308.3	77%	421.1	-12%
Devgen	DEVG	163	218	12.4	28%	19.1	34%	-22.0	-112%	Geron	GERN	370	159	2.8	-63%	53.7	-2%	-62.0	-69%
DiagnoCure	CUR	26	64	0.9	-79%	5.5	50%	-11.8	-77%	Gilead Sciences	GILD	46,563	3,441	5,335.8	26%	721.8	22%	2,011.2	25%
Discovery Laboratories	DSCO	113	118	4.6	NA	26.6	1%	-39.1	2%										

(continued)

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Table 9 List of public biotech companies (continued)

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				(\$ M)	% change	(\$ M)	% change	(\$ M)	% change					(\$ M)	% change	(\$ M)	% change	(\$ M)	% change
GNI <sup>c</sup>	2160	10	88	1.8	-3%	2.0	-48%	-12.5	-22%	Lexicon Pharmaceuticals	LXRX	192	347	32.3	-36%	108.6	4%	-76.9	-31%
GPC Biotech	GPCB	90	59	16.4	-31%	22.2	-67%	-28.2	71%	Life Technologies	LIFE	4,041	9,700	1,620.3	26%	142.5	23%	31.3	-78%
GTC Biotherapeutics	GTCB	33	156	16.7	20%	21.0	-27%	-22.7	38%	Lifecycle	LCP	95	106	30.3	163%	48.2	48%	-26.7	6%
GTx	GTXI	612	147	13.5	90%	44.3	15%	-51.8	-28%	Ligand Pharmaceuticals	LGND	260	73	27.3	112%	30.8	-31%	-98.1	-135%
Halozyme Therapeutics	HALO	456	129	8.8	131%	44.2	115%	-48.7	-104%	Liponex	*LPX	NA	NA	NA	NA	NA	NA	NA	NA
Hana Biosciences	HNAB	8	33	0.0	-100%	18.4	-13%	-22.2	15%	Lorus Therapeutics	LOR	10	29	0.1	18%	4.8	-11%	-9.6	15%
Harvard Bioscience	HBIO	81	308	88.0	6%	4.0	9%	1.7	224%	Luminex	LMNX	886	384	104.4	39%	18.6	21%	3.1	213%
Helicos BioSciences	HLCS	8	71	0.8	39%	24.6	-1%	-45.7	-24%	MannKind	MNKD	349	580	0.0	100%	250.4	-2%	-303.0	-3%
Helix BioPharma	HBP	82	0	3.9	15%	6.1	49%	-8.4	-11%	Map Pharmaceuticals	MAPP	143	98	0.0	NA	59.3	89%	-72.9	-82%
HemaCare	HEMA	3	217	37.6	10%	0.0	NA	1.0	113%	Martek Biosciences	MATK	1005	569	356.8	28%	27.0	10%	38.6	199%
Hemagen Diagnostics	HMGN	1	30	6.2	63%	0.1	19,589%	-0.6	-227%	Maxygen	MAXY	332	72	100.7	335%	46.3	-23%	30.3	161%
Henderson Morleyb	HML	5	9	0.1	NA	0.4	-8%	-0.7	11%	Medarex	MEDX	716	488	52.3	-7%	194.9	-2%	-38.5	-42%
Heska	HSKA	13	312	81.7	-1%	2.0	-27%	-0.9	-102%	Medgenicsb	MEDG	5	10	0.0	NA	1.6	268%	-3.0	-186%
Hollis-Eden Pharmaceuticals	HEPH	20	42	0.0	-100%	16.1	-12%	-21.6	7%	Medi-Cult	MEDC	56	211	36.2	44%	3.4	12%	2.4	271%
Human Genome Sciences	HGSI	287	880	48.4	16%	330.6	0%	-244.9	7%	Medigene	MDG	203	133	52.4	66%	36.3	-2%	-40.7	-3%
Hybrigenics	ALHYG	29	45	5.7	28%	NA	NA	-8.5	-7%	Medivir	MVIRB	146	99	12.0	-61%	NA	NA	-12.2	-239%
IBEX Technologies	IBT	1	21	2.8	53%	-0.1	-104%	0.9	140%	Meridian Bioscience	VIVO	1027	411	140.1	25%	6.7	35%	30.8	55%
Icagen	ICGN	25	72	12.3	-42%	22.1	-21%	-14.8	-36%	Mesoblast	MSB	76	2	0.7	-46%	4.5	-2%	-7.2	-15%
Idenix Pharmaceuticals	IDIX	327	173	10.0	-85%	53.9	-37%	-70.2	15%	Metabasis Therapeutics	MBRX	11	52	4.8	-47%	36.4	-11%	-42.3	-1%
Idera Pharmaceuticals	IDRA	179	37	26.4	230%	16.2	22%	1.5	111%	Metabolic Explorer	METEX	154	95	4.3	15%	9.1	65%	-0.5	-123%
IDEXX Laboratories	IDXX	2,149	4,700	1,024.0	11%	70.7	5%	116.2	24%	Metabolix	MBLX	292	98	1.6	-8%	24.7	24%	-36.0	-29%
IDM Pharma	IDMI	40	16	3.1	-78%	11.2	-50%	-18.6	-1%	MethylGene	MYG	8	86	29.5	90%	30.3	-13%	-7.3	67%
Illumina	ILMN	3223	1,536	573.2	56%	100.0	35%	50.5	118%	Micromet	MITI	221	114	27.3	48%	39.2	34%	-33.2	-65%
Immtech Pharmaceuticals	IMM	65	7	NA	NA	NA	NA	NA	NA	MiddleBrook Pharmaceuticals	MBRK	130	352	8.8	-15%	19.1	-13%	-41.6	2%
ImmuCell	ICCC	5	31	4.6	-24%	1.7	11%	-0.5	-171%	Migenix	MGI	7	32	0.1	257%	3.5	-45%	-8.5	37%
Immunogen	IMGN	218	210	34.5	-8%	60.8	33%	-41.3	-118%	Millipore	MIL	2,846	5,900	1,602.1	5%	102.6	-4%	145.8	7%
Immunomedics	IMMU	128	39	15.3	50%	23.1	14%	-14.4	20%	Miraculins	MOM	1	0	0.0	NA	0.3	-52%	-0.9	39%
Incitive	ICV	2	NA	0.1	-45%	0.7	-11%	-1.2	54%	MolMed	MLM	163	91	5.2	4%	NA	NA	-23.1	-37%
Incyte	INCY	368	212	3.9	-89%	146.4	40%	-178.9	-106%	Mologen Holding	MGNG	78	44	0.3	40%	5.8	7%	-8.1	6%
Infinity Pharmaceuticals	INFI	192	161	83.4	240%	47.5	40%	23.7	240%	Momenta Pharmaceuticals	MNTA	461	167	14.6	-32%	55.3	-21%	-62.6	9%
Inhibitex	INHX	11	34	3.2	12%	12.5	25%	-13.2	68%	Monogram Biosciences	MGRM	59	382	62.2	44%	23.8	23%	-11.7	50%
Innate Pharma	IPH	57	88	9.7	-15%	25.0	-2%	-13.0	-10%	Monsanto	MON	38,547	21,700	11,365.0	91%	980.0	-100%	2,024.0	-100%
InSite Vision	INSV	19	35	13.7	-42%	16.2	56%	-21.3	-485%	Morphosys	MOR	417	334	94.8	16%	36.5	24%	17.4	15%
Insmed	INSM	57	97	11.7	54%	21.0	10%	-15.7	22%	Myriad Genetics	MYGN	3081	994	386.6	192%	123.5	27%	96.6	329%
Inspire Pharmaceuticals	ISPH	204	250	70.5	45%	44.6	-16%	-51.6	19%	Nabi Biopharmaceuticals	NABI	174	40	0.0	NA	12.6	-33%	-10.7	-123%
Intercell	ICLL	1374	248	68.0	8%	74.2	39%	22.7	243%	Nanogen	NGEN	12	248	46.9	23%	18.7	-30%	-38.1	-12%
Intercytex	ICX	14	50	0.0	NA	13.2	-6%	-15.2	1%	Nanosphere	NSPH	106	116	1.4	17%	23.7	10%	-37.0	30%
Interleukin Genetics	ILI	6	27	10.0	3%	3.6	22%	-6.7	-7%	Napo Pharma		0	21	NA	NA	NA	NA	NA	NA
Ipsogen	ALIPS	30	48	5.5	NA	1.8	NA	-1.5	NA	Nastech Pharmaceutical	NAPL	11	44	2.6	-86%	36.8	-30%	-59.2	-13%
Isis Pharmaceuticals	ISIS	1,375	300	107.2	84%	106.4	36%	-12.0	91%	Nektar Therapeutics	NKTR	514	338	90.2	-67%	154.4	1%	-34.3	-5%
Isolagen	ILE	7	13	1.1	-21%	10.2	-24%	-31.4	12%	Neogen	NEOG	367	447	112.3	41%	4.0	28%	13.5	70%
Isoteknika	ISA	10	41	4.7	104%	11.3	-62%	-15.7	54%	NeoPharm	NEOL	5	20	0.0	NA	4.8	-24%	-8.2	25%
Ista Pharmaceuticals	ISTA	24	225	83.1	41%	32.4	0%	-30.7	20%	Neose Technologies	NTEC	19	50	NA	NA	NA	NA	NA	NA
Karo Bio	KARO	135	63	1.3	42%	20.8	-11%	-21.5	14%	Neurobiological Technologies	NTII	8	8	14.3	-20%	27.5	5%	-19.1	-38%
Keryx Biopharmaceuticals	KERX	10	16	1.3	31%	38.0	-52%	-52.9	41%	Neurocrine Biosciences	NBIX	124	125	4.0	225%	55.3	-33%	-88.6	57%
										Neurogen	NRGN	10	30	0.0	-100%	31.6	-48%	-34.3	38%

(continued)



Table 9 List of public biotech companies (continued)

Company Name	Ticker	Market cap (\$ M) <sup>a</sup>	Number of employees	Sales		R&D		Net Inc		Company Name	Ticker	Market cap (\$ M) <sup>a</sup>	Number of employees	Sales		R&D		Net Inc	
				(\$ M)	% change	(\$ M)	% change	(\$ M)	% change					(\$ M)	% change	(\$ M)	% change	(\$ M)	% change
NeurogesX	NGSX	21	42	0.0	NA	16.1	-36%	-26.0	19%	Phynova	PYN	2	6	0.0	NA	1.0	-34%	-2.9	31%
Neurosearch	NEUR	272	242	14.3	-34%	53.1	15%	-69.4	-40%	Physiomics	PYC	2	6	0.1	-58%	0.2	-15%	-0.6	-125%
Newron Pharma	NWRN	84	38	2.3	-35%	11.3	52%	-14.4	-48%	Phytopharm	PYM	11	30	3.8	-16%	6.2	-43%	-3.3	61%
Nicox	COX	578	133	4.4	-84%	98.3	54%	-97.8	-130%	Poniard Pharmaceuticals	PARD	67	62	0.0	NA	34.7	49%	-48.6	-48%
Northfield Laboratories	NFLD	27	91	0.0	NA	16.9	-32%	-22.1	26%	Prana Biotechnology	PRAN	30	11	0.4	-4%	4.1	28%	-9.7	-22%
Norwood Immunology	NIM	4	5	0.2	110%	0.5	-28%	-20.5	-486%	Prima Biomed	PRR	15	1	0.0	-63%	0.1	-93%	-1.4	40%
NovaBay Pharmaceuticals	NBY	22	31	6.7	14%	9.6	29%	-8.1	-50%	Probi	PROB	45	19	8.4	56%	NA	NA	1.0	-67%
Novavax	NVAX	131	70	1.1	-30%	24.3	38%	-36.0	-4%	Progenics Pharmaceuticals	PGNX	314	242	67.7	-11%	85.1	-11%	-44.7	-2%
Novogen	NOVG	33	68	9.6	-23%	13.5	17%	-17.8	-2%	ProMetic Life Sciences	PLI	35	120	10.2	20%	14.6	-19%	-16.4	27%
NPS Pharmaceuticals	NPSP	294	47	102.3	19%	19.0	-48%	-31.7	-641%	Pro-Pharmaceuticals	PRW	2	0	0.2	NA	0.0	NA	-6.7	NA
Nucrist Pharmaceuticals	NCST	17	106	20.9	-31%	5.0	-21%	-3.0	26%	Proteome Sciencesb	PRM	54	40	1.2	309%	NA	NA	-3.4	1%
Nuvelo	NUVO	16	83	15.3	-67%	27.8	-35%	-29.9	-143%	Protox Therapeutics	PRX	463	654	578.1	-25%	59.7	-23%	-47.8	-196%
Nventa Biopharmaceuticals	*NVN	2	8	0.0	-100%	5.4	-19%	-7.1	43%	Qiagen	QGEN	3,190	3,041	893.0	37%	97.3	50%	89.0	78%
Nymox Pharmaceutical	NYMX	102	16	0.4	3%	2.2	-23%	-4.6	13%	QLT	QLTI	180	135	124.1	-3%	29.6	-23%	134.9	223%
Octopus	OCTO	32	144	22.4	226%	NA	NA	-8.2	59%	Quidel	QDEL	425	322	128.1	9%	11.1	-13%	18.8	38%
Oncolytics Biotech	ONCY	0	16	0.0	NA	10.9	-13%	-14.3	11%	ReGen Biologics	RGBO	24	17	1.4	39%	4.0	2%	-10.0	4%
Oncomethylome	ONCOB	117	57	4.0	15%	14.6	3%	-13.5	-2%	Regeneron Pharmaceuticals	REGN	1,462	938	238.5	91%	278.0	38%	-82.7	22%
Oncothyreon	ONTY	16	18	40.0	953%	10.6	-13%	7.1	135%	RegeneRX Biopharmaceuticals	RGN	61	10	0.2	-30%	7.1	-20%	-10.6	5%
Onyx Pharmaceuticals	ONXX	1,927	197	194.3	115%	123.7	49%	1.9	106%	Reliance GeneMedix	GMX	3	47	0.0	NA	3.4	-33%	-7.7	6%
Optimer Pharmaceuticals	OPTR	360	61	1.0	33%	29.0	-30%	-35.6	23%	Replidyne	RDYN	25	3	0.0	-100%	27.4	-37%	-41.1	-635%
Oragenics	ORNI	10	5	0.2	75%	2.0	25%	-6.0	-160%	Repligen Corporation	RGEN	118	56	28.1	112%	10.5	78%	5.2	427%
OraSure Technologies	OSUR	169	287	71.1	-14%	19.3	36%	-31.3	-1,365%	Response Genetics	RGDX	12	54	7.1	-9%	2.2	-12%	-9.5	-88%
Orchid Cellmark	ORCH	20	427	57.6	-4%	0.8	-19%	-4.5	-51%	Rigel Pharmaceuticals	RIGL	293	181	0.0	-100%	109.7	56%	-132.3	-78%
Ore Pharmaceuticals	ORXE	3	11	2.0	22%	9.7	-6%	-22.5	35%	Rosetta Genomics	ROSG	39	70	1.5	NA	8.7	36%	-9.5	35%
Orexigen Therapeutics	OREX	192	48	0.1	0%	79.3	58%	-93.2	-61%	Samaritan Pharmaceuticals	SPHC	2	18	NA	NA	NA	NA	NA	NA
Orthovita	VITA	257	234	76.9	33%	6.7	4%	-10.8	64%	Sangamo BioSciences	SGMO	143	78	16.2	78%	31.2	22%	-24.3	-13%
Oscient Pharmaceuticals	OSCI	6	316	86.8	9%	2.9	-51%	-64.8	-117%	Sanochemia Pharmazetika	SAC	27	185	39.1	0%	2.0	-49%	-4.9	26%
OSI Pharmaceuticals	OSIP	2251	503	379.4	11%	135.3	10%	471.5	611%	Santhera	SANN	148	81	0.0	-99%	27.7	35%	-39.3	-60%
Osiris Therapeutics	OSIR	609	158	10.0	390%	69.9	48%	-33.5	38%	Sareum Holdings	SAR	6	33	2.2	-40%	NA	NA	-2.5	-221%
Oxford Biomedica	OXB	87	76	27.0	155%	39.6	22%	-14.7	34%	Savient Pharmaceuticals	SVNT	315	73	3.2	-77%	55.5	9%	-84.2	-73%
Oxigene	OXGN	23	34	0.0	0%	18.4	30%	-21.4	-5%	SciClone Pharmaceuticals	SCLN	34	227	54.1	46%	23.5	35%	-8.3	16%
Pain Therapeutics	PTIE	249	48	63.7	-3%	45.8	-4%	15.3	-24%	Seattle Genetics	SGEN	713	261	35.2	57%	110.9	71%	-85.5	-75%
Palatin Technologies	PTN	8	46	3.7	-80%	15.9	-64%	-15.1	50%	SemBioSys Genetics	SBS	11	43	0.7	-46%	9.6	18%	-18.7	-20%
Panacos Pharmaceuticals	PANC	7	41	NA	NA	NA	NA	NA	NA	Senesco Technologies	SNT	17	18	0.3	-8%	2.1	63%	-6.0	-84%
PCI Biotech	PCIB	6	7	1.1	26%	2.2	-3%	-1.7	-12%	Senomyx	SNMX	86	124	17.2	-6%	31.8	6%	-26.9	-23%
PDL BioPharma	PDLI	739	10	294.3	31%	166.9	-30%	68.4	425%	Sequenom	SQNM	1204	248	47.1	15%	27.5	91%	-44.2	-101%
Peplin	PLI	8	40	0.0	NA	14.1	7%	-18.7	-26%	Silence Therapeutics	SLN	62	46	3.2	-45%	9.8	39%	-10.8	-45%
Peregrine Pharmaceuticals	PPHM	66	131	11.2	372%	17.4	17%	-19.1	7%	Sinovac Biotech	SVA	106	305	46.5	39%	2.8	189%	8.0	5%
PerkinElmer	PKI	1,643	7,900	1,937.5	14%	108.1	4%	126.4	-4%	StemCells	STEM	129	55	0.2	309%	17.8	-11%	-29.1	-16%
PharmaGap	GAP	2	0	0.0	-100%	0.5	-36%	-1.9	21%	Strategic Diagnostics	SDIX	18	168	27.7	2%	3.6	22%	-15.8	-1937%
Pharmasset	VRUS	307	67	1.9	-85%	46.5	330%	-60.8	-1304%	Sucampo Pharmaceuticals	SCMP	241	94	112.1	22%	46.2	46%	25.0	89%
Pharmexa	PHARMX	9	12	1.0	-49%	24.6	-18%	-34.6	-18%	Summit	SUMM	5	147	4.4	193%	12.3	185%	-14.8	-235%
Pharming	PHARM	65	81	0.9	0%	27.7	9%	-34.4	-221%										
Phase Forward	PFWD	537	718	170.2	27%	25.5	27%	13.8	-53%										

(continued)

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Table 9 List of public biotech companies (continued)

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				(\$ M)	% change	(\$ M)	% change	(\$ M)	% change					(\$ M)	% change	(\$ M)	% change	(\$ M)	% change
Sunesis Pharmaceuticals	SNSS	11	36	5.4	-44%	26.3	-27%	-37.2	4%	Tripep	TPEP	2	5	0.5	NA	2.1	-20%	-3.1	24%
SurModics	SRDX	446	254	136.4	94%	41.1	96%	36.2	80%	Trubion Pharmaceuticals	TRBN	23	101	16.5	-18%	31.6	-13%	-25.6	-10%
Sygnis Pharma	LIO	73	43	0.7	70%	7.0	116%	-8.4	-47%	Unigene Laboratories	UGNE	57	103	19.2	-6%	10.4	23%	-6.1	-76%
Symyx Technologies	SMMX	201	540	159.0	27%	75.4	14%	-106.6	-668%	United Therapeutics	UTHR	1455	360	281.5	33%	239.2	187%	-42.8	-315%
Synaigen	SNG	6	23	0.0	-100%	2.9	32%	-3.2	-31%	Vanda Pharmaceuticals	VNDA	13	23	0.0	NA	23.9	-49%	-51.1	31%
Synta Pharmaceuticals	SNTA	208	129	2.6	252%	81.6	57%	-92.6	-46%	Verenium	VRNM	59	303	69.7	51%	63.4	21%	-185.5	-72%
Syntopix	SYN	9	18	0.2	355%	1.5	-25%	-2.1	19%	Vertex Pharmaceuticals	VRTX	4571	1,322	175.5	-12%	516.3	0%	-459.9	-18%
Synvista Therapeutics	SYI	1	0	0.0	NA	0.0	NA	-12.3	-995%	Vical	VICL	57	118	8.0	44%	25.5	11%	-36.9	-3%
Targacept	TRGT	89	114	20.1	74%	41.0	18%	-25.7	9%	Wilex	WL6	57	64	2.6	10%	26.7	-12%	-27.1	8%
Targanta Therapeutics	TARG	13	86	NA	NA	NA	NA	NA	NA	ViRexx Medical	REX	0	26	NA	NA	NA	NA	NA	NA
Targeted Genetics	TGEN	4	58	8.7	-16%	15.2	-14%	-20.7	-28%	ViroPharma	VPHM	1,025	201	232.3	14%	66.3	85%	67.6	-29%
Techno	TECH	2453	693	268.5	27%	23.4	20%	109.1	40%	Vivalis	VLS	141	66	8.1	488%	10.8	48%	0.6	115%
Tekmira Pharmaceuticals	TKM	16	76	11.7	-26%	13.5	59%	-11.6	-349%	VIVUS	VVUS	369	130	102.2	87%	77.0	189%	-9.9	-317%
Thallion Pharmaceuticals	TLN	5	94	0.2	-92%	7.6	-32%	-12.1	73%	WuXi PharmaTech	WX	396	3,172	253.5	87%	NA	NA	-15.0	-144%
Theratechnologies	TH	98	72	0.2	-66%	28.3	-11%	-39.3	-5%	XenoPort	XNPT	681	222	42.0	-63%	83.2	12%	-62.5	-322%
Theravance	THRX	766	191	23.1	5%	82.0	-47%	-93.6	41%	XOMA	XOMA	87	195	68.0	-19%	82.6	25%	-45.2	-267%
Threshold Pharmaceuticals	THLD	9	31	1.4	0%	13.4	-43%	-18.3	40%	XTL Biopharmaceuticals	XTLB	7	5	5.9	-16%	11.9	-101%	-9.3	89%
Thrombogenics	THR	346	46	40.1	2,323%	20.8	-9%	16.0	176%	YM BioSciences	YMI	0	37	5.6	105%	0.0	NA	-10.7	62%
TiGenix	TIG	124	78	0.0	NA	13.2	23%	-20.1	-27%	ZymoGenetics	ZGEN	206	530	74.0	92%	139.1	-9%	-116.2	22%
Topotarget	TOPO	46	68	7.8	-2%	26.1	14%	-53.6	-42%			<b>416,028</b>	<b>194,601</b>	<b>90,218</b>	<b>21%</b>	<b>25,448</b>	<b>12%</b>	<b>3,838</b>	<b>128%</b>
Transgene	TNG	450	214	13.2	-64%	42.7	12%	-23.8	-227%										
Transition Therapeutics	TTHI	0	36	0.0	-100%	13.6	43%	-16.6	6%										
Trimeris	TRMS	30	4	20.6	-58%	5.1	-60%	8.0	-71%										
Trinity Biotech	TRIB	160	711	140.1	-2%	7.5	12%	-77.8	-120%										

Bold-face companies are new IPOs from 2008.

Source: Ernst and Young (Boston) company reports, Nature Biotechnology.

<sup>a</sup> US market caps are as of Dec. 31, 2008; non-US company market caps are as of April or May, 2009; <sup>b</sup> Six-month data; <sup>c</sup> Nine-month data; NA, not available