

William Blair & Company
Limited Liability Company

222 West Adams Street Chicago, Illinois 60606

INVITROGEN CORPORATION

(IVGN)

May 9, 2000
 Basic Report

(00-054)

Winton Gibbons (312) 364-8371 wgg@wmlblair.com
 Adam Chazan (312) 364-8418 amc@wmlblair.com

Price: \$66 1/4 (\$12-\$94 1/8)

Fiscal Year Ends: December

Fiscal Year	Earnings Per Share	Price/Earnings Ratio
1999	\$0.57	NM
2000E	\$0.72	92.0x
2001E	\$0.94	70.5x
2002E	\$1.21	54.8x

Earnings Per Share Growth

1997-1999	55%
1999-2002E	29%

Return on Average Equity

1999	5%
2001E	16%

Book Value Per Share (December 1999): \$3.57
 Sales (1999): \$92.9 million

Insider Ownership: 32%
 Common Shares: 23.3 million
 Market Value: \$1.3 billion

Investment Opinion: Buy

Invitrogen Corporation is a leading supplier of research biochemical kits, products, and services to the growing genomics, proteomics, and broader life-science markets, which we currently value at \$3.4 billion and estimate to be growing 22% compounded annually, with the kit-based subsegment valued at \$425 million and growing 23% annually. As the body of genomics data continues to grow at an exponential rate, and the completion of the human genome appears imminent, researchers seek means to convert raw sequence and gene data into functional knowledge applicable to the pharmaceutical, agricultural, and forensic markets. Invitrogen specializes in developing and supplying proprietary, easy-to-use, and platform-independent molecular biology kits and tools that allow researchers to more rapidly and reproducibly conduct gene extraction, cloning (copying), and expression experiments, as well as protein analysis—all critical elements of functional genomics and proteomics research. The Invitrogenomics service business offers customers the ability to access leading-edge, high-throughput discovery tools and scientists, while providing a test-bed for Invitrogen to develop new products. Invitrogen's innovative product line, global presence, and infrastructure should help to produce about 25% revenue growth excluding acquisitions, leading to almost 30% earnings per share growth compounded annually. Revenue and earnings upside exist as a result of expected complementary and accretive acquisitions, such as the recent acquisitions of NOVEX, the leading supplier of precast electrophoresis gels and tools, and Research Genetics, a leading supplier of DNA probe-based discovery tools, as well as through leveraging the Invitrogenomics service business. We recommend this stock as a primary genomics holding.

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Invitrogen Corporation—Buy

Invitrogen is a leading company supplying kit-based reagents, equipment, and services to the growing genomics market, currently valued at \$3.4 billion and growing 22% compounded annually, with the kit-based subsegment valued at \$425 million, and growing at 23% annually. The company's broad, proprietary product line, coupled with a global marketing presence and an aggressive targeted acquisition strategy, should enable continued leadership in this vital segment of the life-science market.

Summary Income Statement								
(\$ in millions)								
Fiscal years ends December 31	1999	% Revenue	2000E	% Revenue	2001E	% Revenue	2002E	% Revenue
Revenues	\$92.9	100%	\$117.0	100%	\$146.3	100%	\$181.2	100%
COS	32.7	35%	39.1	33%	46.7	32%	54.9	30%
Gross Profit	\$60.2	65%	\$77.9	67%	\$99.6	68%	\$126.3	70%
S&M	16.2	17%	22.4	19%	27.9	19%	33.8	19%
G&A	12.3	13%	15.3	13%	18.1	12%	21.4	12%
R&D	14.7	16%	15.3	13%	19.5	13%	25.3	14%
Total Operating Expense	\$43.2	47%	\$53.1	45%	\$65.5	45%	\$80.5	44%
Operating Income	16.9	18%	24.8	21%	34.1	23%	45.8	25%
Other Income (expense)	1.3	1%	3.9	3%	4.4	3%	4.8	3%
Earnings Before Income Taxes	\$18.2	20%	\$28.7	25%	\$38.5	26%	\$50.6	28%
Income Taxes	6.6	36%	10.2	35%	13.5	35%	17.7	35%
Net Income	\$11.7	13%	\$18.5	16%	\$25.0	17%	\$32.9	18%
Stock adjustments	\$0.7							
Income available	\$12.4		\$18.5		\$25.0		\$32.9	
EBITDA	20.9		\$25.9		\$35.2		\$47.0	
EPS	\$0.57		\$0.72		\$0.94		\$1.21	
Shares Outstanding	21,629		25,846		26,619		27,291	
Year-over-year Growth	1999		2000E		2001E		2002E	
Revenue	31.6%		26.0%		25.1%		23.8%	
Gross Profit	36.3%		29.4%		27.9%		26.8%	
Operating Income	44.6%		46.4%		37.4%		34.5%	
Net Income	64.2%		58.8%		35.1%		31.4%	
EPS	75.5%		24.9%		31.2%		28.2%	

Summary of Balance Sheet				
(\$ in millions)				
	1999	2000E	2001E	2002E
Cash and Equivalents	\$102	\$271	\$288	\$313
Working Capital	\$135	\$289	\$310	\$340
Shareholders' Equity	\$127	\$318	\$344	\$377

Summary of Cash Flows				
(\$ in millions)				
	1999	2000E	2001E	2002E
Net Cash Provided by Operations	\$11	\$11	\$23	\$30
Net Cash Used in Investing	\$0	(\$5)	(\$5)	(\$5)
Net Cash Provided by Financing	\$89	\$162	(\$1)	(\$1)
Net Cash Increase (Decrease)	\$100	\$168	\$18	\$25

Source: Company financials; FactSet; William Blair & Company, L.L.C. estimates

Quarterly EPS				
	1999	2000E	2001E	2002E
1Q	NA	\$0.18A	\$0.20	
2Q	NA	\$0.17	\$0.23	
3Q	NA	\$0.19	\$0.25	
4Q	\$0.16	\$0.19	\$0.26	
Year	\$0.57	\$0.72	\$0.94	\$1.21

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Summary of Investment Recommendation: Buy

Invitrogen is a leading supplier of research biochemical kits, products, and services to the growing genomics, proteomics, and broader life-science markets, which we currently value at \$3.4 billion and estimate to be growing 22% compounded annually *with the kit-based subsegment valued at \$425 million, and growing at 23% annually*. As the body of genomics data continues to grow at an exponential rate and the completion of the human genome is imminent within weeks, researchers seek means to convert raw sequence and gene data into functional knowledge applicable to the pharmaceutical, agricultural, and forensic markets. Invitrogen develops and sells kit-based molecular biology reagents. These proprietary, easy-to-use, and platform-independent products allow researchers to more rapidly and reproducibly conduct critical experiments (gene extraction, cloning, and expression experiments, as well as protein analysis) enabling functional genomics and proteomics research. The Invitrogenomics service business offers customers, such as Novartis, the ability to access leading-edge, high-throughput discovery tools and scientists, while providing a test-bed for Invitrogen to develop new products. Invitrogen's innovative product line, global presence, and infrastructure should help to produce more than 25% growth internally, with upside from future acquisitions, as demonstrated by the recent acquisitions of NOVEX, the leading supplier of precast electrophoresis gels and tools, and Research Genetics, a leading supplier of DNA probe-based discovery tools. Therefore, we recommend Invitrogen as a primary genomics holding.

Our investment recommendation for Invitrogen is on the basis of the following factors:

1) We believe the market for reagents for use in the life-science market is highly attractive.

Genomics, the applied study of genetic information, focuses on improving the manner in which drugs are discovered and developed, improving agricultural practices and results and ensuring greater security with forensic applications. Genomics accomplishes this by deriving fundamental genetic information that can serve to direct research into gene function, such as functional genomics and proteomics. The kit-based research reagent market constitutes an attractive subsegment of the genomics market, estimated at \$425 million and growing 23% annually. Overall, the development and supply of research tools and reagents represents an attractive market opportunity, estimated to be \$3.4 billion in 2000 and growing 22% annually.

2) Invitrogen is a leading company and well positioned to capitalize on this important, growing market.

Invitrogen's broad product offering, complementary to other genomic technologies provided by companies such as PE Biosystems and Celera Genomics Group, caters to most of the critical processes related to functional genomics and proteomics research. The company's core competencies lie in developing proprietary, technology-focused kit-based reagents that enable tremendous efficiencies and are easy to use. The company employs an aggressive technology licensing and development program to acquire, integrate, and leverage a large technology portfolio—yielding a tremendous array of differentiable, value-added, and niche-filling products. The multi-pronged distribution strategy and an experienced management team round out Invitrogen's strengths.

3) The company should enjoy open-ended-growth opportunities as a transformer of technologies into proprietary products; a high-value service provider; and a consolidator of niche products and companies.

Future acquisitions and a value-added service business should provide potential revenue upside. The fragmented nature of the research reagent market provides a consolidator of technologies, products, and companies with many profitable, high-growth acquisition targets, whose products may complement Invitrogen's already large offering. The recent acquisitions of NOVEX, a leading supplier of proteomics tools, and Research Genetics, a

leading supplier of high-margin, oligonucleotide-based functional genomics products, validate this strategy. The fledgling Invitrogenomics service business hopes to leverage the company's high-throughput cloning technology to participate in another area of the value chain, by offering high-throughput cloning services to pharmaceutical and biotech customers.

4) We expect the company to achieve roughly 30% EPS growth for the near future.

We expect Invitrogen's earnings growth to be driven by almost 25% revenue growth across its three major product segments—gene cloning, gene identification, and gene product analysis, as well as through operating leverage. In addition, potential revenue upside resulting from acquisitions of technologies and companies, as well as continued operational improvements in both existing and acquired businesses, should spur earnings growth.

5) In our opinion, Invitrogen has valuation upside, considering its market position and opportunities.

An analysis of comparable life-science reagent supply companies reveals that companies in this subsegment of genomics are priced 2.5 times their 2001 price-to-earnings-to-growth rate. At current levels, Invitrogen trades in line with the group. *However, valuation seems to ignore the potential revenue upside and acceleration attainable through acquisitions and the Invitrogenomics service business.*

Risks

Government funding/National Institutes of Health (NIH) budgets. A U.S. House panel in December 1999 approved a biomedical spending increase of 14.7% for fiscal 2000, bringing appropriations to \$17.9 billion. Trends in genomics' earmarked funding, particularly focused on extracting the full benefit of various genome projects, remain positive. The National Human Genome Research Institute (NHGRI) may be used as a proxy for flow of government funds into genomics. Funding obligations to the NHGRI as a proportion of spending increased 8% compounded annually, to 1.9% of total NIH expenditures in 1999, from 1.4% in 1995, representing 15% compounded annual growth from 0.7% in 1990. Government funded research centers steadily have increased to 17 centers in 1999, from 15 in 1995 and 4 in 1990. President Clinton in a briefing concerning the NIH budget focused on exploiting genomic discoveries through continued investment in information technology related to genomics. Currently the company maintains a 50/50 split between research revenues, which is defined as all academic and government related research, and rapidly growing commercial revenues, which includes pharmaceutical and biotechnology spending. In total, all NIH funded researchers represent the company's single-largest account, accounting for 6% of the company's worldwide revenue. Invitrogen's large and diverse customer base provides sufficient insulation from any adverse funding event that may dampen NIH related spending. In addition, international government funding trends continue to favor increasing genomic research funding. Using five of Japan's government ministries as a proxy, biotechnology funding increased more than 45% in 2000. Lastly, an increasing portion of Invitrogen's business is derived from nongovernment funded sources such as pharmaceutical and biotechnology companies, as well as agribusiness and diagnostic firms.

Technological obsolescence. Reliance on well-accepted methods could create a risk of being blindsided by new technologies from existing competitors or new upstarts. The company's focus on protected, leverageable technology—rather than product development strategy—combines technologies, thereby extending the life cycle of individual technologies.

Intellectual property/commodity. Reliance on well-accepted methods and the porous nature of the life-science supply market, provides somewhat low barriers to entry from existing competitors or new upstarts. Invitrogen's aggressive technology licensing strategy has led to the accumulation of an impressive intellectual property portfolio that the company has been able to leverage across its product line, leading to the creation of proprietary products.

While competition for technology licenses may increase as market participants troll for new technologies in the same pond, Invitrogen's existing relationships with academic technology transfer offices provide the company with experience in dealing with such agencies, as well as visibility to better access technologies at favorable terms. The stacking of several technologies into a single product component enhances the value of each technology, while the bundling of these components into procedure-specific kits counters some of these competitive pressures.

Integration of acquisitions. Merging businesses of any size is not easy, with possible disruptions occurring in all aspects of the business, ranging from manufacturing to sales. We expect management to rely on extensive previous experience to navigate these changes, minimizing disruptions while maximizing the operational efficiencies that may be achieved. Invitrogen's acquisition of NOVEX was followed by a 14% reduction in headcount and a move of some manufacturing operations, thereby creating operating efficiencies, eliminating redundancies, and reducing overhead.

Genomics backlash. Currently there are discussions in Europe and Japan to label and, in some cases, ban genetically modified (GM) food or organisms (GMOs). In addition, there are serious ethical considerations regarding the use of human genomics information, especially during assisted reproduction or for health insurance purposes. While the rational consideration of these issues should be of great importance to all of us, we believe that the possibility of a genomics backlash will have limited long-lasting effects for three reasons. First, there are billions of people outside the highly developed countries who desperately need medicines and food that this technology could provide. Second, we believe many environmentalists should become allies to genomics once they realize they would make trade-offs (e.g., between destruction of rain forests for farmland, devastation of coral reefs due to overuse of pesticides and fertilizers, and the filling up of landfills with plastics that are not biodegradable, versus avoiding these catastrophes by leveraging genomics). Third, addressing these issues requires substantial information, which likely will be enabled by products such as those provided by Invitrogen.

Market volatility. The fascination with genomic technologies and the promised fruit it may yield has led to an increased level of investor exuberance, without full understanding of technologies and business models. Indiscriminate buying seems to have led to fickle investors for many of the companies in the genomics sector, contributing to volatility. As exemplified on March 14, 2000, comments by President Clinton regarding public access to publicly funded genomics products precipitated a collapse of the entire stock market. A minor retraction of these comments contributed to a significant bounce back, with no change to the underlying fundamentals of the market or individual businesses. A large institutional shareholder base—currently constituting 59% of shareholders—should lend stability.

Weak news flow. Genomics companies typically are characterized as news-driven, rather than earnings-driven, stocks. While Invitrogen has an impressive record of profitability and earnings growth, its position in the genomics value chain as a supplier of discovery tools may be a detriment to the company's stock valuation. The lack of milestones and resulting weak news flow may result in an apparent drowning out of Invitrogen by event-/concept-driven stocks in the genomics space, such as Celera Genomics Group. The company may be able to mitigate this risk by highlighting both its participation in a revolution by supplying the essential "wet" picks and shovels required to undertake discovery research and its innovative Invitrogenomics service business, which participates further along in the genomics value chain.

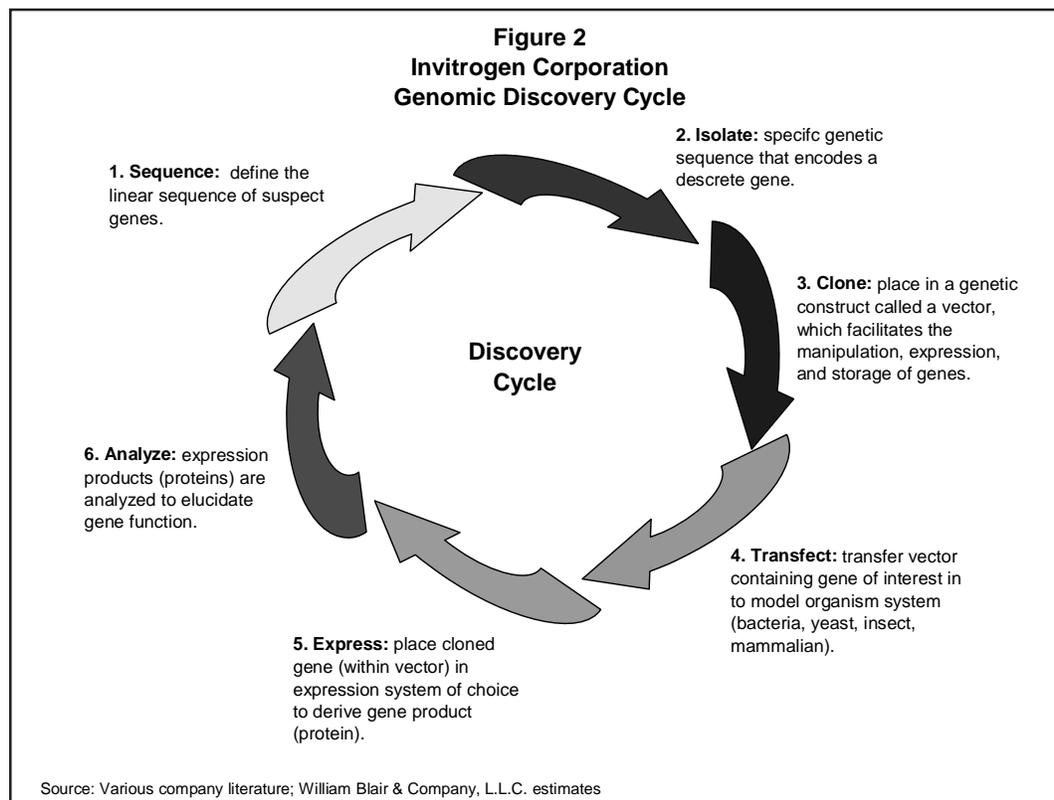
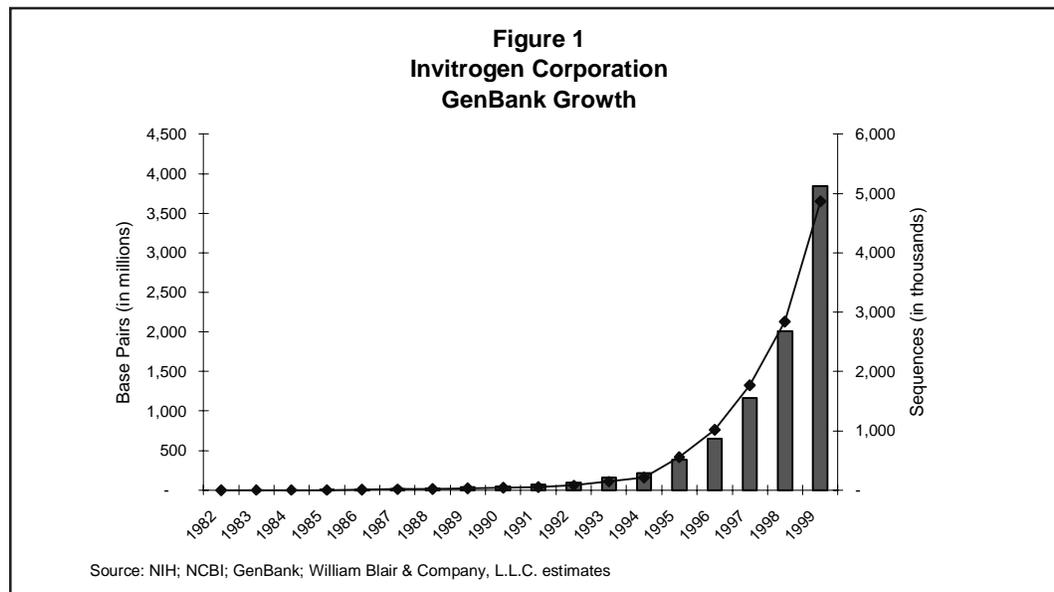
Genomics Represents an Important, Growing Market

Genomics, the applied study of genes, promises to improve quality of life through its application in the important areas of pharmaceuticals, farming, and forensics. The goal of pharmaceutical and biotechnology companies is to create drugs to improve health, while simultaneously generating sufficient return to investors. These groups are finding their current portfolios of drug-discovery tools inadequate to meet these goals, and soon will be faced with a therapeutic pipeline gap. The agribusiness industry has achieved great strides in improving the yields of crops through traditional breeding programs and the use of chemical pesticides and fertilizers. Yet as the worldwide population continues to grow—with estimates topping 7.5 billion in 2010—such benefits cannot be attained in developing areas where the resources to implement these technologies are nonexistent and malnutrition persists. A by-product of population growth is the increase in urban crowding, creating the likelihood of heightened criminal activity.

Genomics should improve the drug-discovery process by using genetic information to elucidate the molecular basis of disease, and by doing so, generate many thousands of validated targets that then can be processed using high-throughput screening systems and other technologies to derive more-effective therapies. By deciphering the genetic information critical to agriculture in both crops and pests, organizations can determine which traits to selectively breed to attain yield and fitness goals, or develop safer and more-effective pesticides—both of which are critical in meeting the needs of developing nations. In addition, DNA fingerprinting should provide an even more effective method of identifying and verifying individuals.

Sequencing efforts fueling the genomics discovery engine are powered by the work of companies such as Celera, as well as publicly funded projects such as the Human Genome Project and The Institute for Genome Research (TIGR). Genetic sequence data provide the foundation for genomics research. Raw sequence is accumulating at an exponential rate, as shown in figure 1, on the following page, which uses GenBank as a proxy for the worldwide stockpile of genetic information. The completion of various organisms' sequencing projects only will accelerate the expanding library of information. The use of powerful computers running sophisticated algorithms elucidates the location and infers the function of genes in this growing haystack. Computational analysis conducted by Celera on the recently completed fruit fly genome revealed 13,601 genes, which when expressed may give rise to hundreds of thousands of proteins. The human genome is estimated to contain between 100,000 and 150,000 genes, giving rise to an estimated 1 million proteins. However, computational estimation of gene function from digital data only hints at its utility. Scientists from both public and private research projects must *physically manipulate* the genes under investigation to understand a gene's function alone and as part of a biological system's greater whole. For that matter a gene must be placed (cloned) in a container, called a cloning vector, in order to be easily manipulated.

Researchers use a variety of molecular biology tools to isolate, amplify, and analyze genes and gene products (DNA, RNA, and proteins) in an iterative genomic discovery cycle typified in figure 2. Sequence data captured during a sequencing project are analyzed computationally to gain hints at its function. Once a discrete sequence of interest is identified, it may be pulled from a sequencing library, and either run against a screen of genes with predetermined functions to assign "guilt by association" or be cloned into a vector (carrier) that facilitates easier manipulation of the gene. This vector carrying the gene of interest then may be inserted (transfected) into an experimental biological system (bacterial, yeast, insect, or mammalian cell) expression system of the researcher's choice, which allows for the production of the gene's product or amplification of the clone itself into many copies. These gene products may be analyzed further to help determine the gene's function, leading one to repeat the cycle with the resulting incremental functional information.



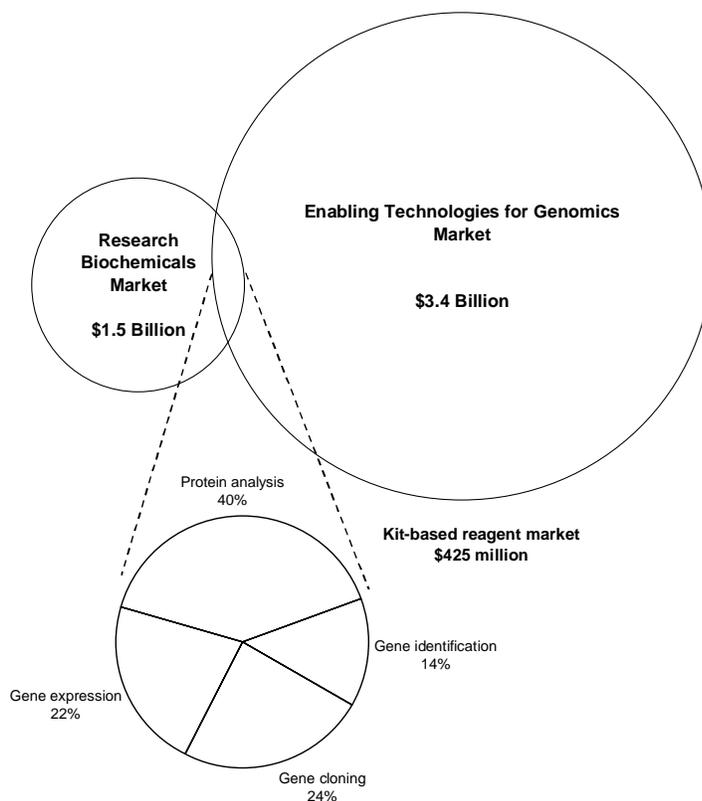
As the rush to capitalize on this information accelerates in a genomics land-grab phase, we anticipate genomics-related *pharmaceutical* research and development expenditures, both internal and purchased, to increase from \$2.6 billion in 2000, to \$9.0 billion in 2005, as shown in table 1. A diverse group of companies supplies the instruments and reagents that facilitate this process, constituting an aggregate market estimated to be \$3.4 billion in 2000 and growing 22% compounded annually, as shown in table 2. More specific, researchers use efficient and easy-to-use, kit-based reagents at each step in this process, constituting an estimated \$425 million market in 2000, growing an estimated 23% compounded annually, to \$1.2 billion in 2005. The market for kit-based reagents may be subdivided into four segments—genetic identification, gene cloning, gene expression, and protein analysis, as shown in figure 3.

Table 1
Invitrogen Corporation
Estimated Pharmaceutical Research and Development Spending

Total												
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Discovery	17.5	19.4	21.6	25.0	29.1	33.7	39.2	45.5	52.8	61.3	71.2	82.7
Development	37.5	41.6	46.2	50.2	54.4	58.9	63.7	68.7	73.9	79.4	85.0	90.7
Total R&D	\$55.0	\$61.1	\$67.8	\$75.2	\$83.5	\$92.7	\$102.9	\$114.2	\$126.7	\$140.7	\$156.2	\$173.3
Percentage of Spending												
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Discovery	32%	32%	33%	35%	36%	38%	40%	42%	44%	46%	48%	50%
Development	68%	68%	67%	65%	64%	62%	60%	58%	56%	54%	52%	50%
Total R&D	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Genomics												
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Discovery	1.8	2.2	2.7	3.5	4.6	5.9	7.7	10.1	13.1	17.0	22.1	28.8
Development	0.4	0.5	0.6	0.7	0.9	1.0	1.3	1.5	1.8	2.2	2.6	3.2
Total R&D	\$2.1	\$2.6	\$3.3	\$4.2	\$5.4	\$7.0	\$9.0	\$11.6	\$14.9	\$19.2	\$24.8	\$31.9
Penetration												
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Discovery	10%	11%	13%	14%	16%	18%	20%	22%	25%	28%	31%	35%
Development	1%	1%	1%	1%	2%	2%	2%	2%	2%	3%	3%	3%
Total R&D	4%	4%	5%	6%	7%	8%	9%	10%	12%	14%	16%	18%
Year-over-year Growth												
	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Discovery		24%	24%	30%	30%	30%	30%	30%	30%	30%	30%	30%
Development		24%	24%	22%	21%	21%	21%	21%	21%	20%	20%	20%
Total R&D		24%	24%	29%	29%	29%	29%	29%	29%	29%	29%	29%

Source: Various company financials; Industry interviews, William Blair & Company, L.L.C. estimates

Figure 3
Invitrogen Corporation
Market Size



Source: Company financials; The Scientist; Frost and Sullivan; Theta Corporation; Business Communications Company; Life Tech; ABRF; Genetic Engineering News; Phrma; Instrument Business Outlook; Phortech; William Blair & Company, L.L.C. estimates

Table 2
Invitrogen Corporation
Enabling Technologies for Genomics Market
(\$ in millions)

Worldwide	1995	1996	1997	1998	1999	2000E	2001E	2002E	2003E	2004E	CAGR (95-98)	CAGR (99-04E)
PCR	360	400	445	495	550	715	895	1,075	1,210	1,325	11%	19%
Total Sequencing	340	400	480	590	750	900	1,090	1,400	1,720	2,120	20%	23%
Other Relevant Reagents and Equipment*	217	255	300	353	415	494	588	699	832	990	18%	19%
Merger Costs	200	255	330	350	420	500	600	720	865	1,040	20%	20%
HTS**	130	145	165	200	290	380	500	655	860	1,125	15%	31%
Proteomics Instruments and Reagents	113	149	196	258	340	422	523	648	804	997	32%	24%
Total Enabling Technologies for Genomics and Molecular Biology	\$1,360	\$1,604	\$1,916	\$2,246	\$2,765	\$3,411	\$4,196	\$5,198	\$6,291	\$7,597	18%	22%
Segment Mix	1995	1996	1997	1998	1999	2000E	2001E	2002E	2003E	2004E		
PCR	26.5%	24.9%	23.2%	22.0%	19.9%	21.0%	21.3%	20.7%	19.2%	17.4%		
Total Sequencing	25.0%	24.9%	25.0%	26.3%	27.1%	26.4%	26.0%	26.9%	27.3%	27.9%		
Other Relevant Reagents and Equipment*	15.9%	15.9%	15.6%	15.7%	15.0%	14.5%	14.0%	13.5%	13.2%	13.0%		
Bioinformatics	54.0%	15.9%	17.2%	15.6%	15.2%	14.7%	14.3%	13.9%	13.7%	13.7%		
HTS**	9.6%	9.0%	8.6%	8.9%	10.5%	11.1%	11.9%	12.6%	13.7%	14.8%		
Proteomics Instruments	8.3%	9.3%	10.2%	11.5%	12.3%	12.4%	12.5%	12.5%	12.8%	13.1%		
Year-over-year Growth of Enabling Technology for Genomics and Molecular Biology		17.9%	19.5%	17.2%	23.1%	23.4%	23.0%	23.9%	21.0%	20.8%		

*Includes DNA synthesis and gene expression

**Does not include assay development and screening services

Sources: Company financials; The Scientist; Frost and Sullivan; Theta Corporation; Business Communications Company; Life Tech; ABRF; Genetic Engineering News; Phrma; Instrument Business Outlook; Phortech; William Blair & Company, L.L.C. estimates

Well Positioned to Supply Value-added Tools for the Genomics Revolution

Invitrogen is a leading company in the development and supply of proprietary, kit-based reagents to manipulate and analyze genes and gene products. The company specializes in supplying innovative, kit-based, life-science reagents that enable the functional analysis of genes. An aggressive intellectual property licensing strategy enables the company to innovate and differentiate its product line, while multiple distribution channels and an experienced management team contribute additional strength.

Innovative, Value-added Product Line Addresses Ubiquitous Needs

Invitrogen develops and distributes innovative high-quality, kit-based, molecular biology research reagents critical for conducting the “wet lab” work necessary for explaining the functional nature of genes in functional genomics and proteomics studies. In essence, molecular biology reagents represent the point at which the rubber meets the road in genomics, by providing the physical tools that translate digital genomic data from large-scale sequencing projects—such as those conducted by Celera and the Human Genome project—into material on which a scientist can conduct functional analysis. An iterative discovery cycle underlies the genomic process (see figure 2, on page 8). Invitrogen’s products target the ubiquitous steps in the experimentation process—gene identification, cloning, expression, and analysis—thus catering to a large and diverse segment of the research community, while maintaining a platform-neutral position complementary to the efforts of genomics companies such as Celera, Incyte, Millennium, and Human Genome Sciences.

Invitrogen’s broad product line spans the breadth of mandatory molecular biology techniques, including gene identification, cloning (for future amplification, storage, and transfection, and analysis (protein purification and analysis). The discovery cycle most often begins with sequence data of some form. Out of this sequence, a researcher must identify the discrete portion that encodes a functional gene. To facilitate this, cDNA (complementary DNA) libraries that represent the essential elements of a gene are created using the mRNA (messenger RNA) transcripts. The library of unknown elements then may be screened against a collection of genes, whose function was previously characterized, with the hopes of determining function by association. Invitrogen’s FastTrack 2.0 kit allows for the rapid isolation of mRNA in *just three hours, rather than three days*, while the cDNA Cycle kit efficiently converts the isolated mRNA into cDNA for additional study. To further simplify the reverse transcription (backward translation) of short-lived mRNA to stable cDNA, the company offers the TriClone system, which combines these steps in an optimized kit.

Once a gene has been identified, the scientist usually places it in some kind of construct that facilitates manipulation, amplification, and storage. The gene typically is placed in a vector, a round piece of DNA containing unique sequences that allow for its use in other techniques. Enzymes are used to precisely “cut and paste” genes and vectors together. Invitrogen offers a wide array of value-added cloning products such as the Zero Blunt, Echo, and TOPO TA kits, commanding market-leading share. The resulting clone containing the gene of interest then may be transfected into an expression system to translate genes into mRNA and subsequently proteins. Expression systems rely on unique vectors that work with particular model organisms such as bacteria, yeast, insect, and mammalian cells that are optimized for each, and may allow for variable study depending on the application. Invitrogen’s T-Rex system is just one of many examples of expression products that allow for the inducible expression of genes with the use of the antibiotic tetracycline in mammalian cells. Other expression products include the pShooter, which features a sequence that directs gene products to particular areas of the cell for functional studies, and the Milk Expression vector kits, which allow for protein production in the milk of transgenic animals for use as therapeutics.

Additional analysis of the gene and its products is performed to identify, quantify, and associate the function of a given gene. Proteins are identified and quantified using a technique called electrophoresis, the use of electricity passing through a gel matrix to separate mixtures of proteins based on size and electrical charge. Typically researchers 'pour' or cast these gels from a mixture of toxic chemicals, which have to be made well ahead of time, and often yield inconsistent results. The company's market-leading NOVEX electrophoresis products are simple kits that researchers can just pull off the shelf, use, and attain consistent, high-quality results. The GeneStorm collection of validated, full-length, and expression-ready clones allows researchers rapidly to derive gene products related to the gene under study for comparative study. These clones free researchers from having to fish out the genes and express them, leading to more efficient discovery.

Invitrogenomics' High-throughput Cloning Business Leverages Market-leading Technology and Expertise

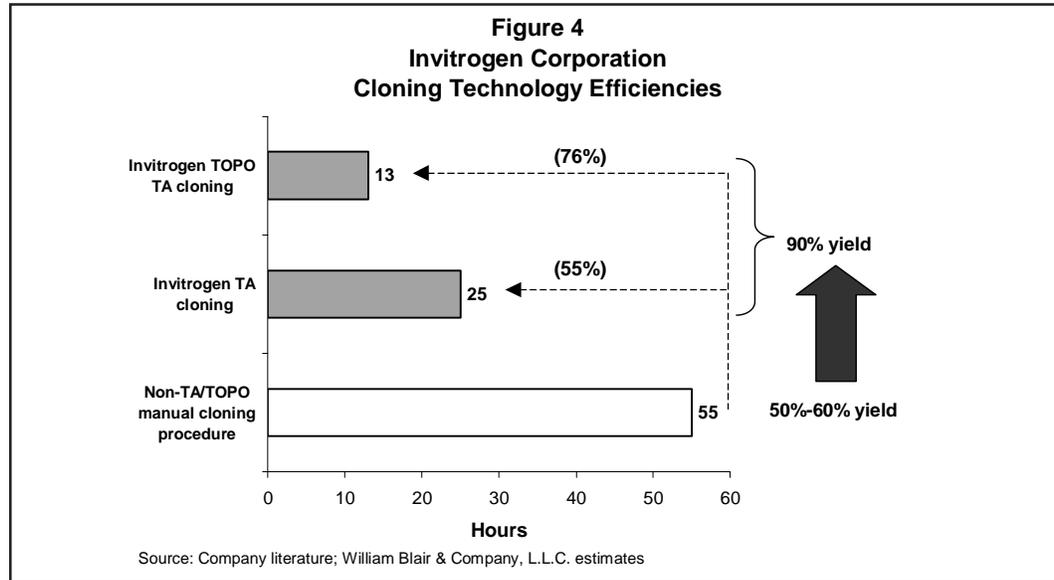
The company is implementing a high-throughput gene cloning and expression business called Invitrogenomics, which is based on the proprietary TOPO TA cloning technology and in-house expertise. The company plans to use its technology to rapidly clone and express tens of thousands of full-length genes and their encoded functional proteins, creating a proprietary library that could be sold and licensed to corporate partners. Invitrogen plans to offer access to these technologies and facilities as an outsourced discovery service in light of increasing genomic research that relies on these fundamental technologies. These cloning strategies are difficult to implement at a scale sufficient for other large-scale projects pursued by pharmaceutical, biotechnology, and agriculture companies. The service business allows Invitrogen to participate in the high-value, downstream discovery work currently being pursued by other genomics companies in other areas. In addition, discoveries made as part of Invitrogenomics efforts may propel additional reagent kit usage by customers, in efforts to harness the resulting information or just to be competitive, and may provide new technology/product opportunities.

Invitrogenomics currently has 17 employees primarily involved in research and development, and manufacturing. The division is currently involved in four collaborations with Novartis, Diversa, Emerald BioStructures, and two unnamed parties. Invitrogenomics's relationship with Diversa began in May 1999 and is expected to yield products based on the collaboration in the near future. The collaboration with the Novartis Institute for Functional Genomics announced in December 1999 validates the Invitrogenomics service offering. As part of the collaboration, Novartis will gain access to Invitrogen's Echo and TOPO TA cloning technologies, around which the company will build a high-throughput cloning facility. In return, Invitrogen will receive the rights to commercialize the reagents and gene clones resulting from these efforts. The company recently entered into a government-funded collaboration with Emerald Biostructures and Molecular Simulations, with the goal of developing simplified methodologies and products for use in crystallographic proteomics studies.

Intellectual Property Acquisition Strategy Promotes Innovation

While the research biochemical reagents market is competitive, we believe that Invitrogen's kits have garnered a high-quality reputation among researchers. The company sells proprietary, technology-laden products bundled as easy-to-use kits. These kits enable once-difficult experiments to be conducted with cookbook-like results, while offering researchers accurate results, as well as substantial time and cost-savings. The TA and TOPO cloning technologies are prime examples of the efficiencies that Invitrogen's products afford researchers. The proprietary TA cloning technology harnesses a unique property of the Taq polymerase enzyme—used to amplify DNA sequences under study—that adds a single A to the top and bottom strand of the amplified sequence, creating overhangs. These overhangs allow for the easy pasting or cloning of the desired sequence into a recipient vector. This simple addition of a single nucleotide *quickly eliminates five additional steps* in the cloning process. Invitrogen's TOPO technology uses a unique property of yet another enzyme, DNA topoisomerase I, to incorporate the amplified gene rapidly into a cloning

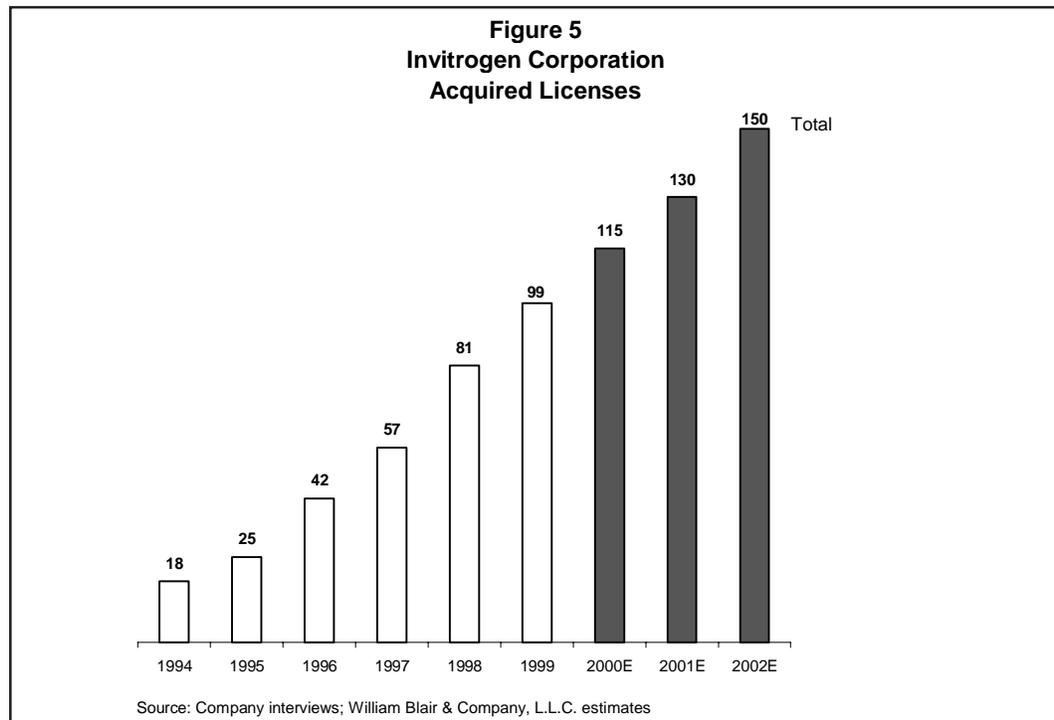
vector, eliminating several steps that require long incubation times (some even *overnight*), and instead substituting a mere *five-minute* incubation. Combining these two technologies creates significant efficiencies, allowing for cloning experiments to be conducted in *less than 13 hours with yields higher than 90%*, versus *55 and 50%-60%, respectively*, using traditional methods, as shown in figure 4. This grants Invitrogen the leading position of the cloning technology market.



Invitrogen is able to offer this innovative, value-added product line by following an aggressive intellectual property licensing strategy. Academic institutions provide a breeding ground for basic, life-science research innovations that as stand-alone technologies have little value. The company actively seeks unique life-science technologies that could provide synergy to existing molecular biology research methodologies, and then licenses or acquires them outright through extensive relationships with technology transfer departments at such academic institutions. Invitrogen thereby provides a commercial outlet for academic innovation in areas of basic research that may have been overlooked and underused. As shown in figure 5, on the following page, the company has licensed roughly 100 technologies—38 of which are exclusive—and anticipates acquiring access to 15-20 new licenses annually. The company holds more than 200 patented technologies in various areas and has 32 issued or pending patents itself. Invitrogen’s focus on technologies rather than products allows it to integrate them in various combinations to offer a wide array of proprietary products that cater to the various niches of the life-science market. By executing on this strategy, the company was able to launch 65 new products in 1999, and anticipates launching 50 to 100 new products annually.

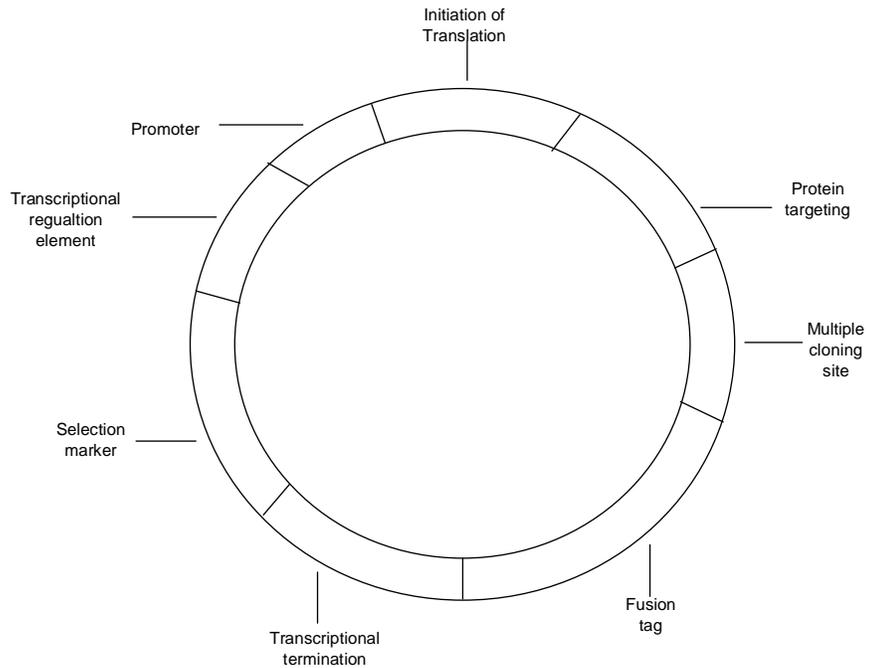
A closer examination of a cloning vector illustrates how Invitrogen puts its technology-licensing strategy and portfolio to work in creating novel products. Cloning vectors are round genetic constructs that trace their origins to small bacterial chromosomes called plasmids. Researchers have incorporated novel elements into the vector, creating a valuable and completely engineerable tool. As shown in figure 6, on page 15, a cloning vector has several prominent elements that are amenable to proprietary design and innovation, promoters, cloning sites, termination sequences, selection markers, targeting sites, and fusion tags. Promoters are sequences of DNA recognized by the cell’s enzymes (RNA polymerase) and enhance the transcription level of the gene into an RNA transcript. This RNA subsequently is translated into proteins, which may be analyzed further. Various combinations of specific sequences (binding sites) are used to induce the desired level of expression in a particular expression system. The initiation of translation or start site is the precise region of sequence that signals the beginning of the gene (ATG-methionine), with

various sequences used to ensure proper transcription. Cloning is accomplished by precisely “cutting and pasting” sample DNA into the vector. The multiple cloning site is a synthetic stretch of DNA that has been designed to include several endonuclease or restriction enzyme (enzyme that cuts DNA when a short, specific sequence is recognized) sites to facilitate the easy insertion of the gene of interest into the expression vector. The enzymes responsible for the translation of DNA require a stop sign to signal the end of a gene and ensure that the proper postscript is added to the mRNA to stabilize it—transcriptional termination sequences accomplish this. Lastly, selection markers are incorporated to select those cells that have taken up and are expressing the vector by exposing growing cells to an antibiotic, thereby allowing researchers to find the proverbial needle in the haystack.



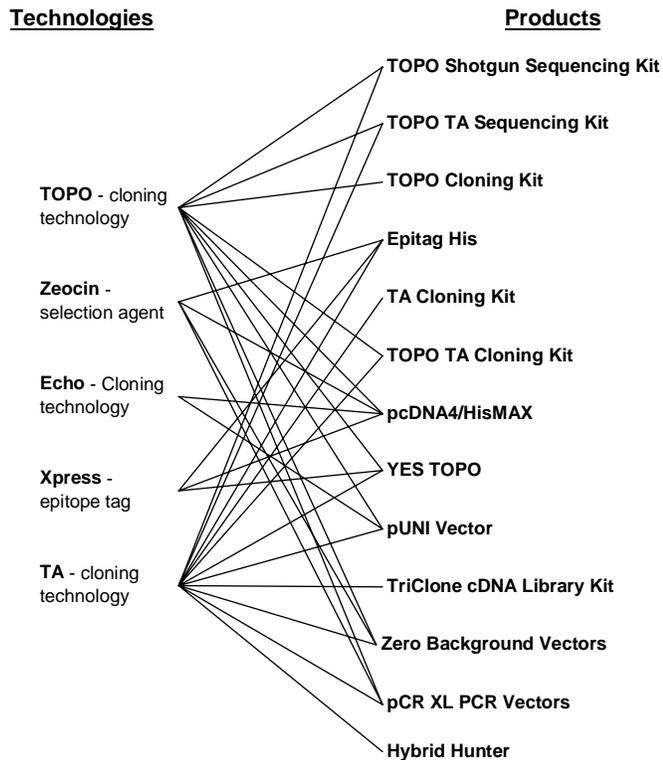
While promoters start/stop and cloning sites are required to ensure the gene will be expressed, protein targeting sites are value-added options that when incorporated inscribe a genetic sequence to direct the resulting protein to a particular structure/location within the cell or instruct the cell to excrete the protein. In certain instances, researchers may want the protein to be embedded in a cell membrane or localized to a particular region within the cell for functional studies. In other instances, excreting the protein outside of the cell makes collecting and purifying the protein for further study or use as a therapeutic easier, by eliminating many costly steps necessary since it is shuttled out into the growth media. Fusion tags, another value-added feature engineered into cloning vectors, are sequences that result in connecting the protein of interest to another protein in order to create a fusion protein. This fused protein allows for easy detection/purification. It is important to note that there are three types of fusion tags: epitope tags for detection using antibodies, reporter tags for visualization or activity analysis, and affinity tags for easy purification. Invitrogen’s ability to access a variety of proprietary cloning technologies that can be mixed and matched in unlimited combinations results in a wide array of unique products, as shown in figure 7.

Figure 6
Invitrogen Corporation
Anatomy of Generic Expression Vector



Source: Principles of Biochemistry; company literature; William Blair & Company, L.L.C. estimates

Figure 7
Invitrogen Corporation
Technology-leveraging Product Development Strategy



Source: Company literature; William Blair & Company, L.L.C. estimates

The research biochemical supply area is crowded with several competitors, large and small, with varying focuses, as shown in table 3. There are broad-line suppliers such as Invitrogen, Life Technologies, Stratagene, and Promega. Others focus on subsegments, such as Qiagen, which targets the nucleic-acid purification market, or Origene, which works on cancer-specific clone libraries. *Invitrogen maintains the broadest product line within its relevant market segments.* In addition, while competitors may offer the individual components needed to perform experiments, Invitrogen's value-added, *kit-based* products enable researchers to move efficiently through the discovery cycle.

Multiple Distribution Channels Successfully Address Fragmented Market

The market for life-science reagents is large and fragmented, comprising both academic and industrial researchers who study a diverse number of systems with both basic and applied interests. Invitrogen maintains more than 5,000 active customer accounts, representing more than 250,000 users worldwide, with approximately half of these customers in the United States. In 1999, the company logged more than 300,000 invoices, with an average order of \$300 each. The largest of these accounts was the NIH, which represents roughly 6% of revenue. Other notable large accounts include Merck, Johnson & Johnson, Amgen, Genentech, and Millennium, with each contributing approximately \$1 million in revenue annually. In an effort to boost sales at these and other larger accounts, the company initiated a freezer program, whereby Invitrogen installs a stocking freezer on customers' premises. This locks in customers and blocks out competitors, and promotes increased use of the products. There currently are about 50 Invitrogen freezers in place at sites that generate \$100,000 to \$200,000 in sales, and the company has targeted up to 50 new sites for future placements.

Invitrogen has developed three established distribution channels—a direct salesforce, direct mail, and a dynamic, e-commerce-ready Web site. A network of 51 (40 in the United States and 11 in Europe) graduate-level-educated, evangelical salespeople attend to accounts worldwide (2 are focused on the massive NIH account alone). The salesforce is supported by a telephone bank currently manned by 13 trained individuals in technical support.

More than 120,000 research groups worldwide receive the company's creative and informative catalog. While recent emphasis has been placed on selling via the Web and the distribution of CD-ROM, a recent study conducted by market research consultant Bioinformatics Incorporated indicated that catalogs remain the most common source for researchers to learn about life-science vendors and their products and are viewed as the primary source of information regarding products and technologies. Other studies conducted by a competing research biochemical supplier support these findings. The catalog's substantial technical content, coupled with its ready pricing information, meet two of the most important criteria elucidated by this study. Invitrogen also publishes the monthly Expressions newsletter, which serves to introduce customers to new products between catalog runs and highlights existing products and their new uses. As with the catalog, Expressions pairs detailed, value-added information often derived from customers with lively presentation, creating an effective marketing tool.

We believe the lively theme in the catalog is carried onto the company's Web site, invitrogen.com, creating strong brand equity for the company's proprietary products. The Web site incorporates all the important features of the catalog—detailed and accessible product information—with the additional functionality of monitored communities to discuss products, technologies, conferences, and other issues. The company believes the entire business should be e-commerce-capable in six to nine months, a feat that the Research Genetics division already accomplished.

**Table 3
Invitrogen Corporation
Molecular Biology Reagent Supply Competitive Matrix**

	Invitrogen	Stratagene	Life Technologies	Clontech (BEC)	Promega	Amersham Pharmacia Biotech	BioRad	Novagen	Origene	Panvera	Roche	Qiagen	Biosource	Techne	Enzo Biochem	
Cloning	Mutiple system	X	X	X												
	PCR cloning	X	X	X	X											
	CDNA synthesis	X	X	X	X											
	Enzymes	X	X	X	X	X	X	X	X		X	X				
Oligonucleotides	Oligonucleotides	X	X	X	X	X							X	X		
Purification	DNA	X	X	X	X	X	X	X	X				X			
	RNA	X	X	X	X	X	X	X	X			X				
	Quantification	X		X					X							
Amplification	PCR optimization kits	X	X	X	X	X			X	X		X				
	RT-PCR	X	X	X	X	X			X	X		X				
	Molecular beacons	X								X						
	Thermocycler		X					X								
Sequencing		X			X					X	X					
Transformation and Transfection	Competent cells	X	X	X	X	X										
	Transfection kits	X	X	X		X							X			
Expression	Physical						X									
	Prokaryotic	X	X	X	X			X		X	X					
	Yeast	X	X	X	X			X		X						
	Insect	X	X	X	X			X								
	Mammalian	X	X	X	X	X		X								
	In vitro					X		X								
	Reporter systems	X	X	X	X	X				X	X					
	Expression ready clones	X	X		X				X							
	Northern blots	X	X		X				X				X			
	Disease specific	X	X		X				X							
Gene analysis/ identification	Yeast two-hybrid	X	X	X					X							
	Bacterial display	X	X													
	Yeast display	X	X					X								
	Mammalian display	X														
	Arrays	X			X	X	X						X	X	X	
	Molecular diagnostics				X	X										
	Molecular identity				X	X										
Protein purification	Standards		X	X	X	X	X	X	X		X					
	Nickle	X								X		X				
	Resin	X								X		X				
Cell culture	Antibody	X	X		X	X	X	X				X	X			
	Selection agents	X		X												
	Media	X		X									X			
Nucleic sample prep	Growth factors		X	X						X				X		
	mRNA	X				X		X			X	X				
Mutagenesis	DNA	X				X		X		X	X	X				
	Vectors	X	X		X	X										
	KO systems		X													
Protein analysis	Precast gels	X	X				X	X								
	Isoelectric products	X					X	X								
	Protein apparatus	X	X	X			X	X								
	DNA apparatus	X	X	X			X	X			X					
	Power supply	X	X	X			X	X								
	Imaging		X	X			X	X								
	Blotting products	X		X	X	X	X	X	X		X					X
	Stains, standards	X			X	X	X	X			X					
Services	X		X		X		X	X			X					
Fine chemicals	X	X	X		X	X	X			X						
Total	43	35	29	25	24	21	16	16	14	14	13	11	6	3	2	

Source: Various company literature, William Blair & Company, L.L.C. estimates

Experienced Management

Invitrogen's management helped build the life-science reagents market from its infancy as well as participated in the business of its customer base. Lyle Turner, president, chief executive officer, and chairman, founded Invitrogen in 1987. Mr. Turner previously held positions at Stratagene, a competitor in the life-science reagent market, and Boehringer Mannheim, now part of Roche. Jim Glynn, senior vice president of corporate development and chief financial officer, has significant experience in the biotechnology arena, having served as chief financial officer of both Matrix Pharmaceuticals and Mycogen Corporation. Lewis Shuster, chief operating officer, has extensive biotech experience as former chief operating officer and chief financial officer of Pharmacopoeia, a combinatorial chemistry company, and the genomics company Human Genome Sciences. Patrick Dillon, chief technical officer, formerly was senior director of genomics at Nanogen, as well as director of gene discovery and exploratory research at Human Genome Sciences. Jim Johnson, vice president of sales and marketing, came to Invitrogen through the NOVEX acquisition, and was formerly at Nichols Institute, and Boehringer Mannheim as vice president of marketing for the highly successful diabetes (blood glucose monitoring) business.

Open-ended Growth Opportunities

While Invitrogen should continue to benefit from participating in the rapidly growing area of genomics, resulting in solid earnings growth, the company faces several opportunities that may serve to strengthen its franchise further. An aggressive acquisition strategy, coupled with a focus on operational efficiencies, as well as a burgeoning service offering, Invitrogenomics, should provide the company with open-ended growth opportunities.

The large, fragmented nature of the life-science reagents market has given rise to many profitable mom-and-pop operations that provide niche products to a limited customer base. Invitrogen hopes to leverage its existing technology, customer base, and sales infrastructure by acquiring high-margin, high-growth companies that have products to expand its offering, while focusing on operational improvements in its existing business to further boost the bottom line. This may be accomplished simply by adding products to the catalog or by following the company's product development strategy and incorporating acquired technologies into existing products. Invitrogen's acquisitions of NOVEX and Research Genetics exemplify this strategy. The expanded product line is appealing to customers because it decreases the number of vendors they must deal with, while the expanded footprint in the space makes Invitrogen a more formidable player and more attractive/prestigious acquirer to entrepreneurs. As shown in table 4, the product lines of NOVEX and Research Genetics dovetailed well with Invitrogen's core line of kit-based reagents. The NOVEX line of precast gels and accessories gives the company added exposure to the burgeoning field of proteomics, while Research Genetics' DNA arrays, molecular beacons, and clone libraries provide added critical mass in the market for premium, value-added functional genomics reagents.

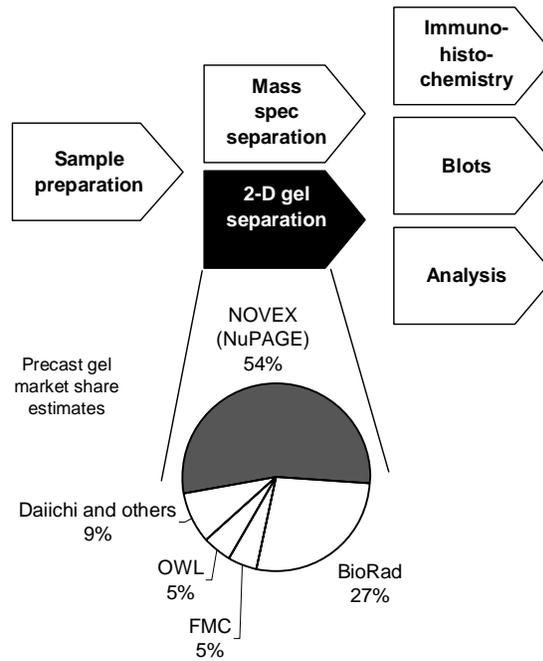
In June 1999, Invitrogen announced the acquisition of NOVEX, a leading developer of supplies used in functional genomics and proteomics, namely precast gels and stains for protein separation, as shown in figure 8. The company's NuPAGE precast gel product line currently enjoys more than a 50% market share, accomplished with a minimal sales effort and exposure. The product features a one-year shelf life without refrigeration, versus the competing product's three-month shelf life, as well as faster run times, as shown in table 5, on page 20, allowing for higher throughput. While NuPAGE gels are more expensive than manually mixing and casting gels, a task typically performed by grad students and lab assistants (i.e., cheap labor), they offer consistent performance in an off-the-shelf manner while avoiding unnecessary exposure to toxic chemicals. Operational improvements at NOVEX should lead margins for this product line to rise to historical Invitrogen levels.

Table 4
Invitrogen Corporation
Complementary Nature of Acquisitions

	Invitrogen	Research Genetics	NOVEX
Cloning	X		
Purification	X		
Amplification	X		
Sequencing	X		
Transformation and transfection	X		
Expression	X		
Gene analysis/identification	X		
Cell culture	X		
Nucleic sample prep	X		
Mutagenesis	X		
Services	X	X	
Oligonucleotide arrays		X	
Molecular beacons		X	
Oligonucleotides		X	
Protein purification			X
Protein analysis			X
1999 revenues	\$38,247	\$24,581	\$30,052

Sources: Company literature; William Blair & Company, L.L.C. estimates

Figure 8
Invitrogen Corporation
Proteomics Value Chain



Source: Various company financials; The Scientist; William Blair & Company, L.L.C. estimates

Table 5
Invitrogen Corporation
Protein Separation Gel Comparison

Buffer System	Typical Run Time (min.)
Tris-Glycine	90
Tricine	70
Novex NuPAGE (Tris-Acetate)	60
Novex NuPAGE (MOPS)	50
Novex NuPAGE (MES)	35

Source: Company literature, William Blair & Company, L.L.C. estimates

In December 1999, the company announced the acquisition of Alabama-based Research Genetics, which added to Invitrogen's position as a leading supplier of functional genomics research tools and services. The company's value-added products include the world's largest collection of documented clone libraries, expression arrays based on these libraries, custom oligonucleotides (short synthesized DNA sequences) for use in DNA sequencing, and molecular beacons (fluorescent DNA probes) for use in real-time PCR (PE Biosystems' TaqMan and Roche's LightCycler) experiments. Researchers are able to buy single clones or entire libraries of clones from Research Genetics over the Internet, in a manner similar to the recently launched Gene-by-Gene program at Incyte Genomics. Research Genetics also offers gene expression services based on the Affymetrix array technology platform. We believe product synergy across the current businesses should soon be realized. For example, Invitrogen may be able to apply its GeneStorm line of clones to Research Genetics' expression arrays, broadening the usefulness of both products.

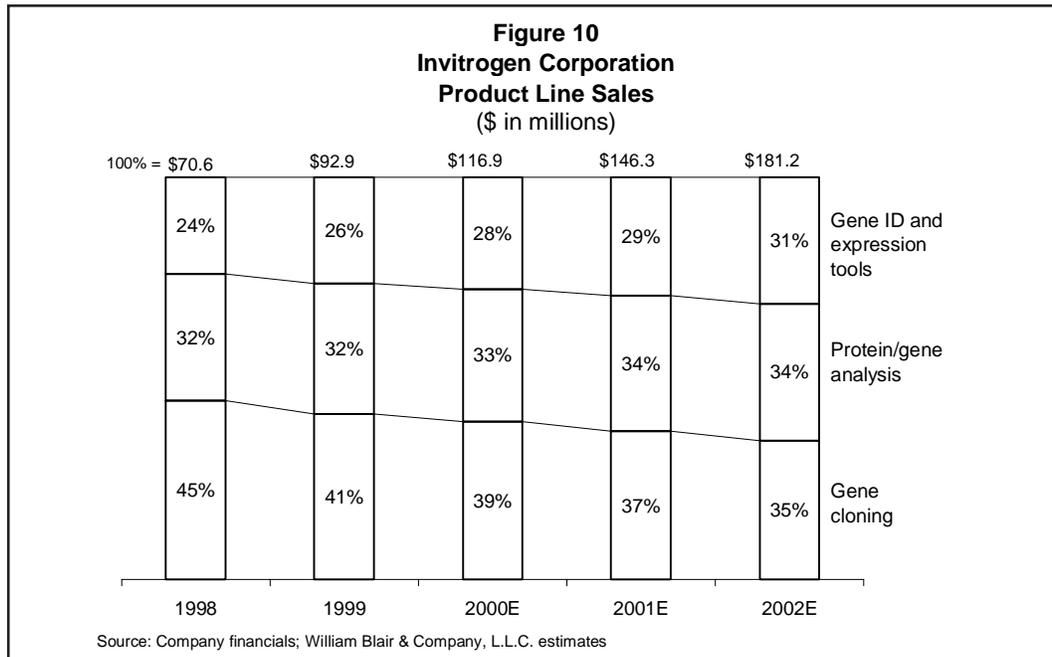
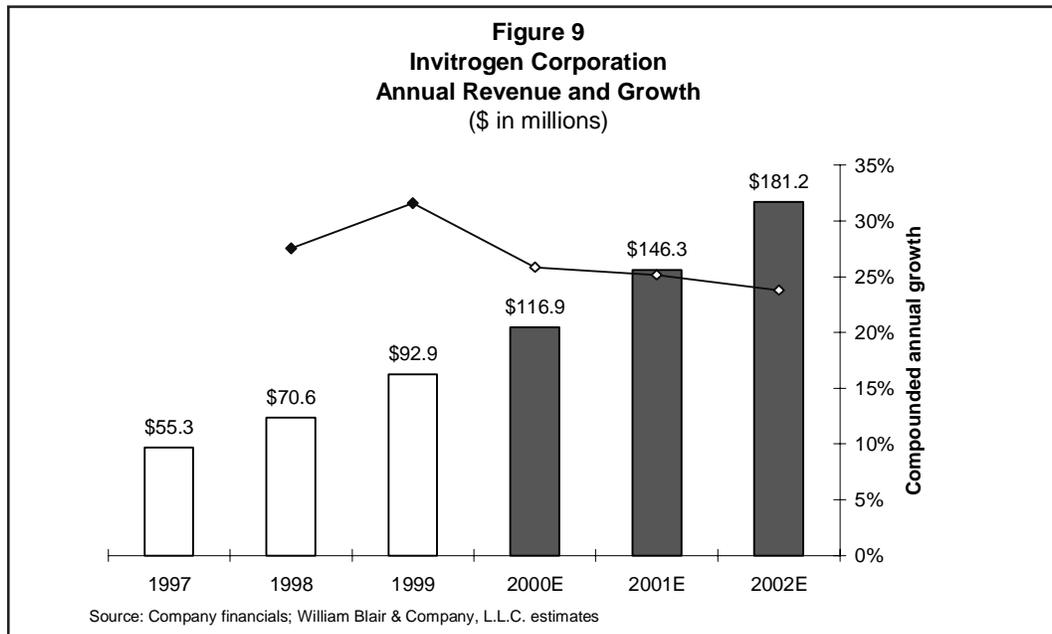
The increasing trend toward outsourcing and high-throughput processes in the pharmaceutical industry presents a growing opportunity for Invitrogen to apply its products and expertise. The company launched Invitrogenomics to provide customers with high-throughput cloning tools and services to help accelerate genomics-based drug-discovery efforts, while simultaneously serving as a test-bed for innovative, new products. The company signed a collaborative agreement with the Novartis Institute for Functional Genomics in the spirit of this service business. The institute will develop a high-throughput cloning facility based on GeneStorm, TOPO, and Echo technology from Invitrogen that should help to strengthen Invitrogenomics. The company's exhaustive contacts and proven record of accomplishment within the pharmaceutical industry should help establish Invitrogenomics as a dominant participant in the genomics service industry.

Roughly 30% EPS Growth Expected

Invitrogen should experience roughly 30% compounded annual earnings per share growth over the next several years. We believe this growth will be driven by strong revenue growth across the three segments of its existing product line—gene identification, gene cloning and expression, and gene product analysis—and by continued operational improvements in existing and acquired businesses. The company may experience earnings upside as additional acquisitions occur and the Invitrogenomics service business attracts customers.

Revenue Should Grow About 25% Annually

We expect revenue to be driven by market growth, new product revenue, and a continued shift toward high-throughput methodologies and away from manual or home-brewed reagents and techniques. The market served by Invitrogen is estimated to be \$3.4 billion and growing 22% compounded annually: defined more narrowly, the market for kit-based, life-science reagents is estimated to be \$425 million, with slightly faster growth of 23%. We expect the company's revenue to grow at least 25% compounded annually, increasing to \$181 million in 2002 from \$93 million in 1999, as shown in figures 9 and 10, and table 6, on page 22.



Revenue from gene cloning, currently the largest contributor to total revenue, should remain strong, increasing to more than \$63 million in 2002 from \$38 million in 1999, as interest in conducting genes discovery fueled by large-scale sequencing projects increases. Products designed to fit the needs of researchers conducting high-throughput studies should help keep Invitrogen at the forefront of research, as well as hasten the acceptance of kit-based reagents over home-brewed reagents. OneShot cells capable of taking up DNA for easy transfection and protein expression now are available in the industry-standard 96-well microplate format, making them amenable for use with robotic liquid handling stations. The Echo univector allows researchers to conduct a single cloning experiment, resulting in genetic constructs that are adapted easily to any expression system, thereby eliminating several previously necessary steps and experiments. Invitrogen's TOPO ShotGun Kit is another example of the company's effort to support high-throughput genomics research. As whole-genome shotgun sequencing gains increasing acceptance with the success of Celera's sequencing efforts on the fruit fly and human genomes, demand for tools that

enable this efficient technique should increase. The TOPO ShotGun kit combines unique tools for shattering genomes into uniform pieces—for an upfront two-hour time savings—with the efficient TOPO cloning technology and competent OneShot cells into a single kit for fast sequencing library creation.

Table 6
Invitrogen Corporation
Product Line Sales
(\$ in thousands)

Revenue	1998	1999	2000E	2001E	2002E
Gene cloning	31,414	38,247	45,896	54,042	62,689
Protein/gene analysis	22,246	30,052	38,587	49,295	61,619
Gene ID and expression tools	16,907	24,581	32,508	42,992	56,857
Total	70,567	92,880	116,991	146,330	181,165
100% of Revenue	1998	1999	2000E	2001E	2002E
Gene cloning	45%	41%	39%	37%	35%
Protein/gene analysis	32%	32%	33%	34%	34%
Gene ID and expression tools	24%	26%	28%	29%	31%
Total	100%	100%	100%	100%	100%
Year-over-year growth	1998	1999	2000E	2001E	2002E
Gene cloning	26%	22%	20%	18%	16%
Protein/gene analysis	37%	35%	28%	28%	25%
Gene ID and expression tools	19%	45%	32%	32%	32%
Total	28%	32%	26%	25%	24%

Source: Company financials; Willaim Blair & Company, L.L.C. estimates

Sales of gene identification and expression tools are estimated to increase to \$57 million in 2002, from \$26 million in 1999, as functional analysis of genes grows. Products such as GeneStorm expression-ready clones, as well as Research Genetics' spotted arrays for expression analysis, should continue to grow more than 30% annually. Of increasing interest should be the company's *Hybrid Hunter line of yeast two-hybrid protein interaction kits*, which facilitate complicated protein studies that are the cornerstone of larger genomics/proteomics companies, such as Curagen.

As proteomics efforts ramp up to better understand proteins and the agents and structures of biology, the demand for consistent, easy-to-use analysis tools likely will increase, in our view. Invitrogen's market-leading position in precast gels through its NOVEX business should experience annual growth of more than 25%, increasing to \$62 million in 2002 from \$30 million in 1999, in our opinion. The company currently offers more than 180 types of gels, which should provide a diverse group of researchers with easy-to-use, consistent gels that meet their precise needs, while simultaneously affording faster run times and extended shelf life.

The company plans to expand its direct sales efforts by increasing the headcount to 50 in the United States from 40, and to 17 from 11 in Europe by the end of the year. The company hopes to increase business in Japan, which historically constituted 7%-8% of revenue. Th country has demonstrated renewed interest in genomics, marked by an increased level of government spending, as shown in table 7. To increase Japanese sales to 15% of revenue, the company hopes to replace the two distributors it currently uses in Japan—Feinkoshi for gene cloning and Yutron for protein analysis—with a direct operation.

**Table 7
Invitrogen Corporation
Japan's Government Biotechnology Budgets 2000**

Ministry	¥ Billion	% Change
Science and technology agency		
Total biotechnology	¥ 69	34%
Genome research	17.6	48%
Development and regeneration project	6.1	New
Brain	201	10%
Ministry of education, science, sports, and culture		
Total biotechnology	42.9	56%
Ministry of international trade and industry		
Total biotechnology	10.4	271%
Bioinformatics	2.3	New
Genome research	6.6	New
Bioresources	1.1	New
Joint collaboration with industry and universities	16.9	100%
Ministry of health and welfare		
Total biotechnology	112	10%
Gene therapy and human genome research	2.6	0%
SNPs	6.1	New
Ministry of agriculture, fisheries, and forestry		
Total biotechnology	18.3	29%
Rice genome	4.1	51%
Green frontier research	5.6	45%

(US \$1 = ¥102)

Source: Nature Biotechnology; William Blair & Company, L.L.C. estimates

The company may experience additional revenue as it acquires businesses in the reagent marketplace that meet its criteria of leading market position, company-level margins, and strong growth of at least 20%. Invitrogen constantly evaluates up to 20 acquisition targets, however the timing of these transactions is difficult to anticipate—although we expect them to be more of the tuck-in variety. Revenue derived from the Invitrogenomics service business also may provide additional revenue growth, although the timing and size of agreements require enhanced visibility beyond current levels. For this reason, we intentionally exclude these revenue estimates from our models.

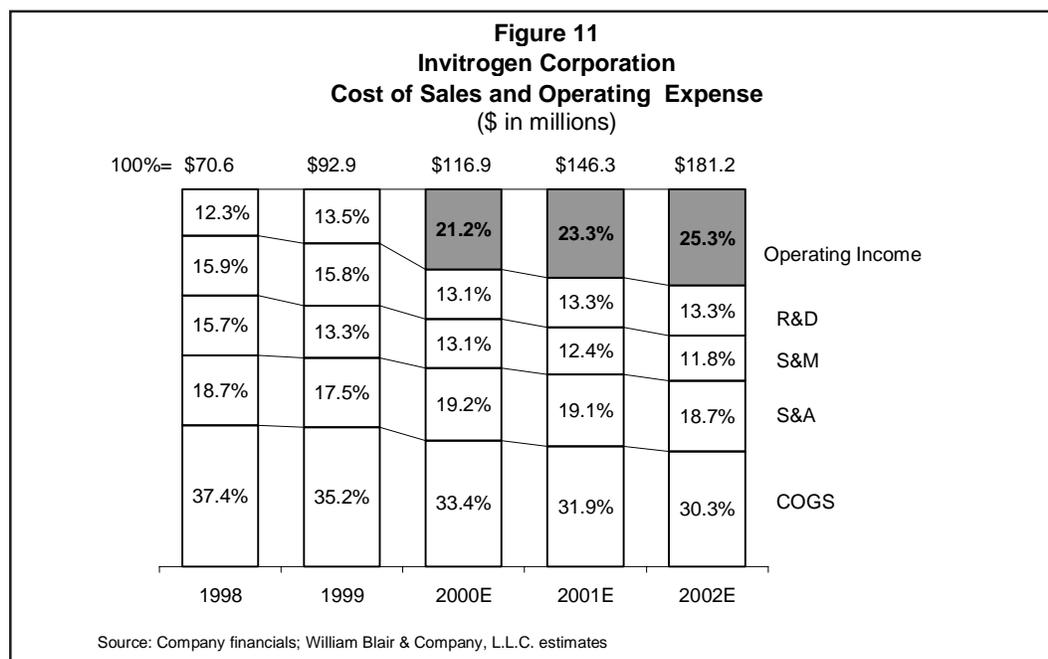
Noticeably absent from our discussion of future revenue is Invitrogen's potential participation with the Internet market makers that target the life-science market. The company has been reluctant to deal with such firms, because it believes its order processing costs, estimated to be 2% of revenue, are substantially below the fees charged, and an Internet sales presence likely will not be critical for at least three years. In addition, the company does not want to put a buffer between it and its customers (an opinion shared by many in this area, despite relationships with online market makers). Furthermore, onsite stocked refrigerators maintain competitive barriers and make it difficult to justify the planning and waiting required by online distribution. However, we believe that the company's Web site is well executed and experiences brisk traffic. The business should be completely e-commerce-capable within six to nine months, with certain portions such as the Research Genetics business already e-commerce ready.

Gross Margins Should Increase Gradually

The company should be able to improve margins consistently to more than 69% in 2002, from 65% in 1999, on the basis of continued streamlining of operations and headcount reduction at NOVEX. Current margin levels of 65% are average for the broad-line life-science, reagent supply cohort, a group including Life Technologies, Stratagene, Clontech, and Invitrogen.

Operating Expenses Should Continue to Decline 700 Basis Points to Less Than 45% of Revenue by 2002

As shown in figure 11 and table 8, we expect operating expenses as a percentage of revenue to decline over the next few years, as investments in general and administrative infrastructure are leveraged over a larger sales base. Research and development expenditures are anticipated to increase and stabilize at roughly 14% of revenue. It is entirely possible that future collaborations as part of the Invitrogenomics efforts may help to fund additional research and development spending. Sales and marketing expenses are expected to rise as the company invests more to build the direct salesforce both domestically and abroad, and should taper over time as a percentage of sales due to resulting revenue. Because of improvements in gross margin and operating expense ratios, we expect operating margin to increase to 25% of revenue in 2002, from 18% in 1999. Operating income is expected to grow more than 50% compounded annually, to \$46 million in 2002 from \$17 million in 1999.

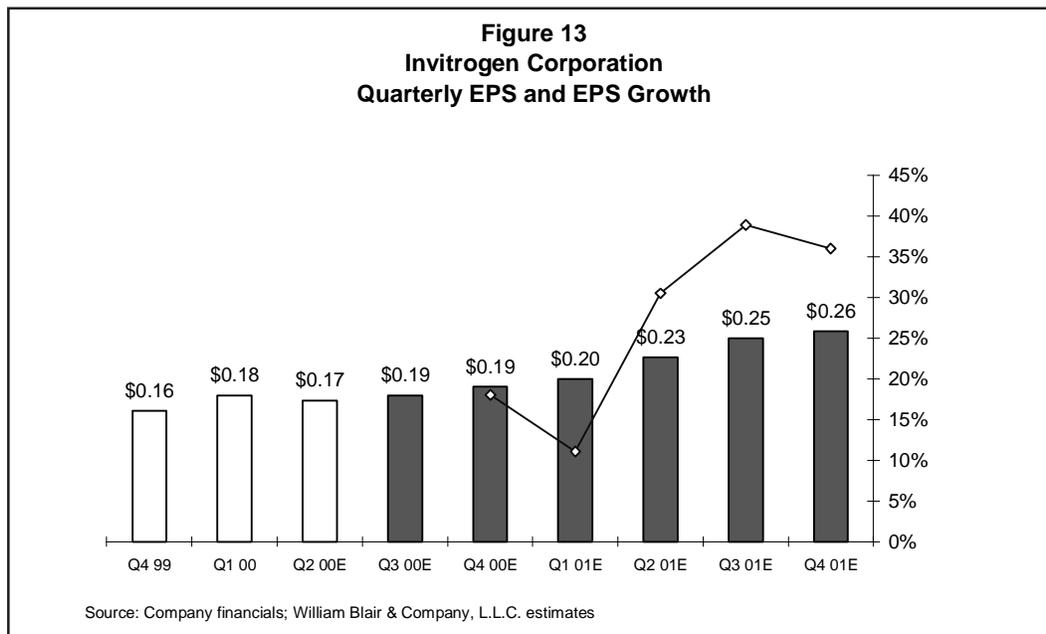
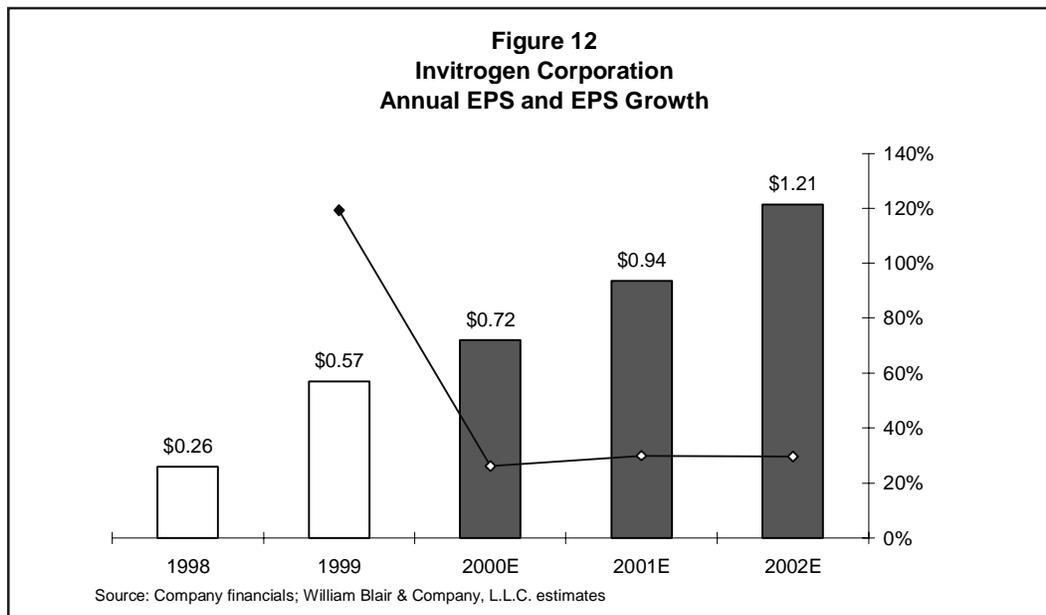


The Tax Rate Should Remain Steady at 36.5%

Earnings Per Share Should Grow Roughly 30% Compounded Annually Through 2002

The improvements in gross margin, operating expenses, and a steady tax rate should result in an increase in net income margin to 18%, or \$33 million, in 2002, from 13%, or \$19 million, in 1999. Earnings per share should increase to \$1.21 in 2002, from \$0.57 in 1999, as shown in figure 12.

Our quarterly estimates are shown in figure 13 and table 9. The revenues should lack the seasonality experienced by companies supplying equipment to researchers, which are at the mercy of budgeting cycles.



Invitrogen’s Balance Sheet and Cash Flow Are Healthy and Should Support a Growing Business

The balance sheet and cash flow, shown in tables 10 and 11, should support our EPS growth estimate of roughly 30%. The recent infusions of cash from the February 1999 initial public offering, the October 1999 secondary offering, and the March 2000 convertible debt offering supplied the company with \$265 million in cash, and we estimate the business should be able to generate roughly \$50 million of additional cash, which may be used to implement its acquisition strategy.

Valuation Upside

Our analysis of comparable life-science, reagent, supply companies indicates that these stocks are priced approximately 2.5 times their 2000 earnings per share estimates to their secular growth rates, as shown in table 12. At current price levels, Invitrogen is in line with the group. However, this valuation appears to exclude the potential upside that future acquisitions and revenue related to its fledgling service business may provide. We anticipate that the addition of another direct comparable in competitor Stratagene, which recently filed a registration statement for an initial public offering, will provide additional insight into Invitrogen's market-leading performance.

Given the company's strong product portfolio focused on key discovery technologies, leading market position in the growing genomics market, and EPS upside provided by acquisitions and service revenues, we rate shares of Invitrogen a Buy.

Additional information is available upon request.

The full text of this report is available in electronic form to registered users via R*Docs™ at www.rdocs.com or www.wmblair.com.

DJIA:	10603.63
S&P 500:	1424.17
NASDAQ:	3669.38

William Blair & Company, L.L.C. maintains a market in the common shares of Invitrogen Corporation.

The prices of the common stock of other public companies mentioned in this report follow:

Affymetrix	\$148 1/8
Genentech	\$131 1/2
Celera Genomics	\$93 3/4
Curagen	\$36 3/4
Diversa	\$33 7/8
Incyte Genomics	\$86 11/64
Johnson & Johnson	\$81 3/4
Millennium	\$81 5/8
PE Biosystems	\$62 3/4

Table 8
Invitrogen Corporation
Annual Income Statement
(\$ in thousands)

Fiscal year ended Dec. 31	1998	1999	2000E	2001E	2002E
Revenue	\$70,567	\$92,880	\$116,991	\$146,330	\$181,165
COGS	26,412	32,690	39,081	46,696	54,853
Gross profit	44,155	60,190	77,910	99,634	126,312
Operating expenses					
Sales and marketing	13,165	16,235	22,442	27,904	33,811
General and administration	11,097	12,311	15,343	18,136	21,358
R&D	11,201	14,699	15,319	19,508	25,304
Total operating expense	35,463	43,245	53,104	65,548	80,473
Operating income	8,692	16,945	24,806	34,087	45,839
Other income					
Gain (loss) on foreign currency	25	(90)	(295)	(239)	(232)
Interest and other expense	(910)	(691)	(3,882)	(3,795)	(3,795)
Interest and other income	1	2,054	8,051	8,444	8,786
Income before taxes	8,507	18,218	28,680	38,496	50,598
Provision for income taxes	2,988	6,558	10,159	13,474	17,709
Net income	\$5,519	\$11,660	18,521	25,022	32,889
Less:					
Preferred stock dividends	(900)	(163)	-	-	-
Accretion of non-voting redeemable common stock	(204)	(74)	-	-	-
Adjustment related to convertible preferred stock		985	-	-	-
Income available to share holders	\$4,415	\$12,408	\$18,521	\$25,022	\$32,889
Diluted earnings per share	\$0.26	\$0.57	\$0.72	\$0.94	\$1.21
Weighted average shares outstanding	17,083	21,629	25,846	26,619	27,291
Year-over-year growth	1998	1999			
Net sales	27.5%	31.6%	26.0%	25.1%	23.8%
Gross profit	35.4%	36.3%	29.4%	27.9%	26.8%
Operating income	55.9%	44.6%	46.4%	37.4%	34.5%
Net income	61.5%	64.2%	58.8%	35.1%	31.4%
EPS		75.5%	24.9%	31.2%	28.2%
	1998	1999	2000E	2001E	2001E
Revenue	100.0%	100.0%	100.0%	100.0%	100.0%
COGS	37.4%	35.2%	33.4%	31.9%	30.3%
Net Cash Increase (Decrease)	62.6%	64.8%	66.6%	68.1%	69.7%
Operating expenses					
Sales and marketing	18.7%	17.5%	19.2%	19.1%	18.7%
General and administration	15.7%	13.3%	13.1%	12.4%	11.8%
R&D	15.9%	15.8%	13.1%	13.3%	14.0%
Total operating expense	50.3%	46.6%	45.4%	44.8%	44.4%
Operating income	12.3%	18.2%	21.2%	23.3%	25.3%
Other income					
Gain (loss) on foreign currency	0.0%	-0.1%	-0.3%	-0.2%	-0.1%
Interest and other expense	-1.3%	-0.7%	-3.3%	-2.6%	-2.1%
Interest and other income	1.0%	2.2%	6.9%	5.8%	4.8%
Income before taxes	12.1%	19.6%	24.5%	26.3%	27.9%
Provision for income taxes	35.1%	36.0%	35.4%	35.0%	35.0%
Net income	7.8%	12.6%	15.8%	17.1%	18.2%
Less:					
Preferred stock dividends	-1.3%	-0.2%	0.0%	0.0%	0.0%
Accretion of non-voting redeemable common stock	-0.3%	-0.1%	0.0%	0.0%	0.0%
Adjustment related to convertible preferred stock	0.0%	1.1%	0.0%	0.0%	0.0%
Income available to shareholders	6.3%	13.4%	15.8%	17.1%	18.2%

Source: Company financials; William Blair & Company, L.L.C. estimates

Table 9
Invitrogen Corporation
Quarterly Statement of Income
(\$ in thousands)

	Q1 00E	Q2 00E	Q3 00E	Q4 00E	Q1 01E	Q2 01E	Q3 01E	Q4 01E
Net sales	\$27,286	\$27,850	\$29,842	\$32,013	\$33,022	\$35,516	\$38,357	\$39,435
Cost of Sales	9,090	9,384	9,979	10,629	10,731	11,342	12,148	12,475
Gross Profit	18,196	18,466	19,863	21,385	22,291	24,174	26,209	26,960
Operating Expenses								
Sales and Marketing	4,778	5,531	5,890	6,243	6,410	6,798	7,265	7,432
General and administrative	3,595	3,726	3,910	4,111	4,205	4,435	4,698	4,798
Research and development	3,521	3,624	3,922	4,252	4,379	4,715	5,112	5,301
Total operating expense	11,894	12,881	13,723	14,607	14,993	15,948	17,075	17,531
Operating Income	6,302	5,586	6,140	6,778	7,298	8,226	9,134	9,429
Other income (expense)								
Gain on foreign currency transactions	(157)	(50)	(30)	(57)	(74)	(53)	(54)	(59)
Interest expense	(1,036)	(949)	(949)	(949)	(949)	(949)	(949)	(949)
Interest and other income	2,005	2,001	2,015	2,030	2,066	2,093	2,122	2,163
Total other income (expense)	812	1,002	1,036	1,024	1,044	1,091	1,120	1,155
Income before provision for income taxes and minority interest	7,114	6,588	7,176	7,802	8,341	9,317	10,254	10,584
Provision for income taxes (benefit)	2,611	2,306	2,512	2,731	2,919	3,261	3,589	3,704
Net income	\$4,503	\$4,282	\$4,664	\$5,071	\$5,422	\$6,056	\$6,665	\$6,880
Diluted EPS	\$0.18	\$0.17	\$0.19	\$0.19	\$0.20	\$0.23	\$0.25	\$0.26
Shares outstanding diluted	25,250	25,779	26,066	26,289	26,420	26,552	26,685	26,818
Net sales	184%	171%	70%	88%	21%	28%	29%	23%
Gross Profit	158%	139%	71%	86%	23%	31%	32%	26%
Operating income	233%	118%	88%	82%	16%	47%	49%	39%
Net income	243%	133%	95%	52%	20%	41%	43%	36%
EPS	10%	42%	38%	20%	15%	37%	40%	33%
	Q1 00E	Q2 00E	Q3 00E	Q4 00E	Q1 01E	Q2 01E	Q3 01E	Q4 01E
Net sales	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Cost of Sales	33.3%	33.7%	33.4%	33.2%	32.5%	31.9%	31.7%	31.6%
Gross Profit	66.7%	66.3%	66.6%	66.8%	67.5%	68.1%	68.3%	68.4%
Operating Expenses	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Sales and Marketing	17.5%	19.9%	19.7%	19.5%	19.4%	19.1%	18.9%	18.8%
General and administrative	13.2%	13.4%	13.1%	12.8%	12.7%	12.5%	12.2%	12.2%
Research and development	12.9%	13.0%	13.1%	13.3%	13.3%	13.3%	13.3%	13.4%
Total operating expense	43.6%	46.2%	46.0%	45.6%	45.4%	44.9%	44.5%	44.5%
Operating Income	23.1%	20.1%	20.6%	21.2%	22.1%	23.2%	23.8%	23.9%
Other income (expense)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Gain on foreign currency transactions	-0.6%	-0.2%	-0.1%	-0.2%	-0.2%	-0.1%	-0.1%	-0.2%
Interest expense	-3.8%	-3.4%	-3.2%	-3.0%	-2.9%	-2.7%	-2.5%	-2.4%
Interest and other income	7.3%	7.2%	6.8%	6.3%	6.3%	5.9%	5.5%	5.5%
Total other income (expense)	3.0%	3.6%	3.5%	3.2%	3.2%	3.1%	2.9%	2.9%
Income before provision for income taxes and minority interest	26.1%	23.7%	24.0%	24.4%	25.3%	26.2%	26.7%	26.8%
Provision for income taxes	36.7%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%	35.0%
Net income	16.5%	15.4%	15.6%	15.8%	16.4%	17.1%	17.4%	17.4%

Source: Company financials; William Blair & Company, L.L.C. estimates

Table 10
Invitrogen Corporation
Balance Sheet
(\$ in thousands)

Fiscal year ends December 31	1999	2000E	2001E	2002E
Assets				
Current assets				
Cash and cash equivalents	\$102,221	\$270,628	\$288,371	\$313,164
Short-term investments				
Accounts receivable	11,335	16,134	20,215	25,129
Inventories	7,490	12,323	16,591	21,412
Income taxes receivable	4,495	5,000	5,000	5,000
Deferred income taxes	3,561	3,817	3,833	3,834
Prepaid expenses and other current assets	1,683	1,424	1,709	2,092
Total current assets	\$130,785	\$309,327	\$335,719	\$370,631
Property and Equipment	29,982	35,390	40,798	46,206
Accumulated depreciation	8,672	9,812	10,952	12,092
Property and equipment, net	21,310	25,578	29,846	34,114
Intangible assets, net	4,471	3,644	3,004	2,364
Other long-term assets	557	3,745	3,187	3,244
Total assets	\$157,123	\$342,294	\$371,756	\$410,353
Liabilities and Group Equity				
Current liabilities				
Note payable to bank	1,385	-		
Current portion of obligations under capital leases	5,242	800	800	800
Accounts payable	4,300	7,270	9,527	12,076
Accrued expenses	9,549	11,685	14,025	17,168
Income taxes payable	1,589	972	1,036	1,032
Total current liabilities	\$22,065	\$20,728	\$25,387	\$31,077
Obligations under capital leases, less current portion	7,256	2,241	1,641	1,041
Deferred income taxes	439	874	1,185	1,533
Commitments and contingencies				
Stockholders' Equity (Defecit)	149			
Common stock	223	291	359	427
Retained earnings (deficit)	127,140	145,661	170,683	203,775
Total stockholder's equity	\$127,363	\$318,452	\$343,542	\$376,702
Total Liabilities and Group Equity	\$157,123	\$342,294	\$371,756	\$410,353

Table 11
Invitrogen Corporation
Statement of Cash Flows
(\$ in Millions)

Fiscal Year Ended Dec 31	1999	2000E	2001E	2002E
CASH FLOWS FROM OPERATING ACTIVITIES:				
Net income	\$6.67	\$18.52	\$25.02	\$33.09
Adjustments to reconcile net income to net cash	0.00	0.00	0.00	0.00
Depreciation and amortization	2.72	1.14	1.14	1.14
Amortization of deferred compensation	0.32			
Employee stock ownership plan contribution				
Deferred income taxes	(0.76)	0.18	0.30	0.35
Non-cash write-off of investments				
Non-cash merger related costs	1.82			
Other non-cash adjustments	0.36			
Changes in operating assets and liabilities:				
Accounts receivable	(1.75)	(4.80)	(4.08)	(4.91)
Inventories	(0.05)	(4.83)	(4.27)	(4.82)
Prepaid expenses and other current assets	(0.07)	0.26	(0.29)	(0.38)
Other assets	0.01	(3.69)	0.56	(0.06)
Accounts payable	(0.68)	2.97	2.26	2.55
Accrued expenses	1.97	2.14	2.34	3.14
Income taxes payable	0.30	(0.62)	0.06	(0.00)
Net cash provided by operating activities	\$10.85	\$11.26	\$23.04	\$30.09
CASH FLOWS FROM INVESTING ACTIVITIES:				
Change in short term investments	4.21			
Payment received on note receivable from officer	0.15			
Purchases of property and equipment	(2.75)	(5.41)	(5.41)	(5.41)
Payments for intangible assets	(1.27)	0.83	0.64	0.64
Investment in related party		0.00	0.00	0.00
Net cash provided by (used in) investing activities	\$0.34	(\$4.58)	(\$4.77)	(\$4.77)
CASH FLOWS FROM FINANCING ACTIVITIES:				
Advances (principal payments) on lines of credit, net	(0.71)	(5.83)		
Proceeds from long term obligations				
Principal payments on long term obligations	(1.41)	(5.01)	(0.60)	(0.60)
Proceeds from sale of common stock	107.94	0.07	0.07	0.07
Proceeds from sale of convertible securities		172.50	0.00	0.00
Redemption of preferred and common stock and payment of accrued dividends	(17.06)	(0.15)		
Net cash provided by (used in) financing activities	\$88.75	\$161.58	(\$0.53)	(\$0.53)
Effect of exchange rate changes on cash	(\$0.05)	\$0.15	\$0.00	\$0.00
Net increase (decrease) in cash and cash equivalents	\$99.90	\$168.41	\$17.74	\$24.79
Cash and cash equivalents, beginning of period	\$2.32	\$102.22	\$270.63	\$288.37
Cash and cash equivalents, end of period	\$102.22	\$270.63	\$288.37	\$313.16

Source: Company financials; William Blair & Company, L.L.C. estimates

Table 12
Invitrogen Corporation
Comparable Company Valuation Analysis

Name	Ticker	05/09/2000	Mkt. Cap.	Calendar EPS Estimates				CAGR			PE Ratio			2000E P/E Growth		William Blair Rating
				1998	1999	2000E	2001E	Secular Growth	2 Year to 2000E	3 Year to 2001E	1999	2000E	2001E	2-Year CAGR	Secular Growth	
Qiagen	QGENF	150.00	\$5,151	\$0.36	\$0.51	\$0.68	\$0.99	38%	37.4%	40.1%	294.1	220.6	151.5	5.9	5.8	
Invitrogen	IVGN	65.50	\$1,654	\$0.17	\$0.57	\$0.72	\$0.94	30%	105.8%	76.8%	114.9	91.0	69.7	0.9	3.0	2
Techne	TECH	77.50	\$1,570	\$0.78	\$0.95	\$1.22	NA	25%	25.1%	NA	81.6	63.5	NA	2.5	2.5	
Life Technologies	LTEK	51.00	\$1,253	\$1.49	\$1.53	\$1.80	NA	NA	9.9%	NA	33.3	28.3	NA	2.9	NA	
Enzo Biochem	ENZ	37.81	\$957	\$0.13	\$0.26	NA	NA	NA	NA	NA	145.4	NA	NA	NA	NA	
Bio Rad	BIO.A	25.75	\$321	\$1.98	\$0.97	NA	NA	NA	NA	NA	26.5	NA	NA	NA	NA	
Biosource	BIOI	5.81	\$48	\$1.10	\$1.32	\$1.65	\$1.95	NA	22.5%	21.0%	4.4	3.5	3.0	0.2	NA	
Median			\$1,253					30.0%	25.1%	40.1%	81.6	63.5	36.3	2.5	3.0	
Mean			\$1,565					31.0%	40.1%	46.0%	100.0	81.4	74.7	2.5	3.8	

Source: Company financials; First Call; William Blair & Company, L.L.C. estimates

Appendix A: Functional Glossary for Genomics Workflows

The science behind genomics may appear daunting given the scale at which it is conducted and the discoveries it enables. The truth is that genomics relies on several common methods that allow researchers to isolate, manipulate, and identify DNA and its relative RNA.

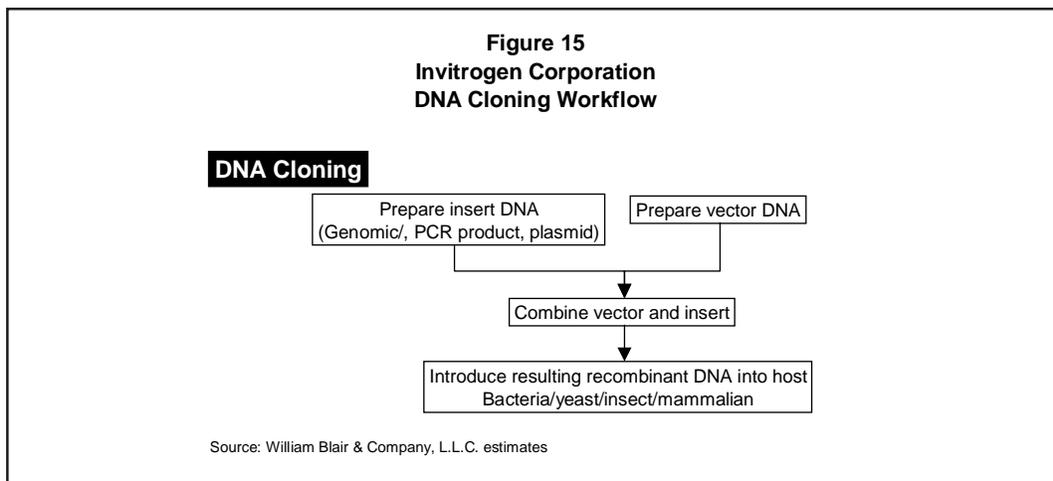
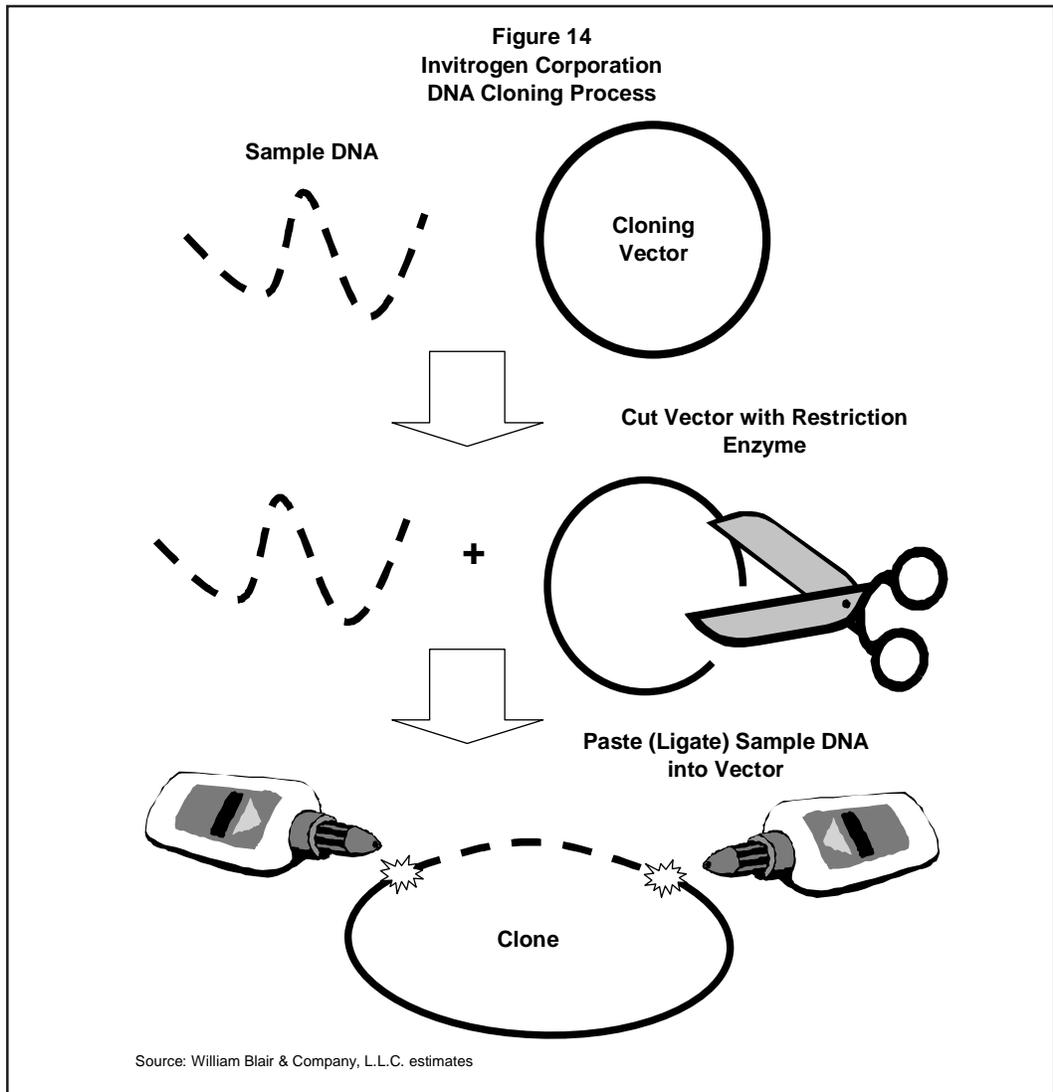
DNA Cloning

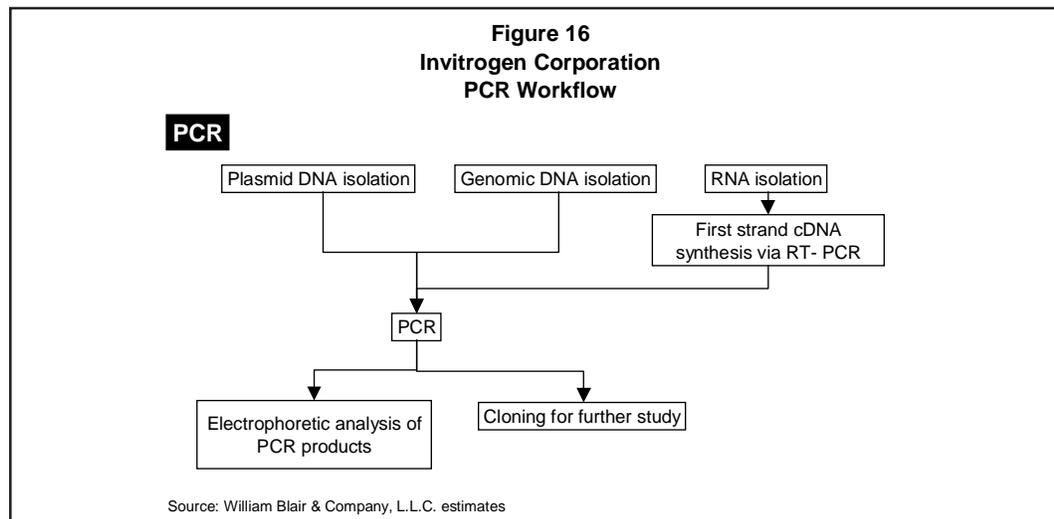
In order to work with DNA it must first be freed from its cellular confines and then meddled with slightly to ease its handling properties. By collecting cells from a specimen, and breaking them open, DNA may be purified from the cell's other contents using chemical or physical methods. The genome of a cell consists of a lot of DNA, which in its entirety is impossible to work with for experiments. It is for this simple reason that researchers seek to break up genomes into smaller, more manageable pieces. This is accomplished through a process known as cloning, which is detailed in figure 14 and 15. DNA from a cellular sample is broken into smaller pieces, which alone are short-lived and difficult to manipulate due to size, amount, and other factors. Researchers use a molecular tool called a cloning vector to make handling and manipulating DNA easier. A cloning vector is a circular piece of DNA, which has incorporated into its sequence unique characteristics that make it amenable for use in research. The naked sample DNA has exposed ends that are attacked by degrading enzymes. By placing the sample DNA in a closed circular construct, the threat of degradation effectively is eliminated. The sample DNA may be modified by enzymatically adding sequences to its ends, which will later serve a recognition function. The cloning vector is cut at a particular sequence site by a restriction enzyme (the scissors). The ends resulting from this cutting are complementary to the modified ends of the sample DNA, which when introduced zip together. An enzyme called a DNA ligase enzyme (the glue) is then added to paste the ends of the DNA together, resulting is a closed circle, called a clone. Often clones of large numbers of DNA fragments will undergo this process to yield a clone library, with each constituent clone containing a unique stretch of sample DNA. The library then may be probed and tested to elucidate experimental hypothesis.

This basic cloning process provides the fodder for additional experimental processes, which are illustrated below.

PCR

The amount of DNA recovered from a sample may be insufficient on which to carry out experiments. Scientists devised a method called polymerase chain reaction (PCR) by which DNA is enzymatically amplified, as shown in figure 16, on page 34. This is accomplished by using the sample DNA as a template which an enzyme called Taq Polymerase, scans and copies, over and over again using heating/cooling cycles until the desired amount is attained. By using fluorescently labeled reagents and coupling the thermocycler instrument to a detection device, researchers are able to monitor the progress of the amplification and extrapolate beginning and ending DNA sample concentrations, a useful tool for gene expression or diagnostic applications, such as measuring viral load in HIV patients.

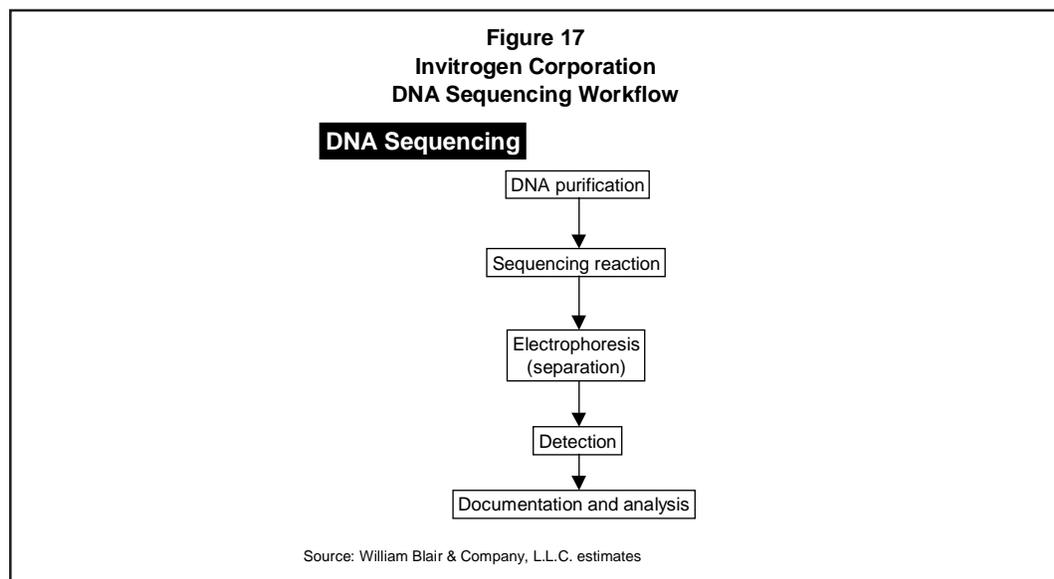




PCR is used to increase the quantity of a sequence and to create cDNA (complementary DNA) or expression libraries or to modify a given sequence by adding restriction (cutting) sites or causing directed mutagenesis. Another important use of PCR is the attachment of fluorescent labels to samples, which is a necessary step in carrying out expression assays such as those using DNA array technology.

cDNA Synthesis

Since the biology of a cell is a dynamic, continuous process, taking snapshots of its activity may provide a wealth of information on how it behaves in response to stimuli and stresses, which could serve as proxies for disease. Since the collection of mRNAs at any given time represents what genes are being turned on/off, studying them under various conditions provides the snapshot. While mRNAs are short-lived and difficult to work with, transcribing them into a more stable, complementary DNA (cDNA) copy allows them to be studied, manipulated, and archived as libraries. The process of creating these libraries is set forth in figure 17. CDNA synthesis exploits an enzyme that is usually involved in the cell's normal DNA repair process, called reverse transcriptase (RT). In a normal chain of events, the central dogma, DNA gives rise to RNA; RNA gives rise to functional proteins. RT reverses the first step in the process, using the mRNA as a template to create a cDNA copy, which then can be cloned into a vector and made part of a cDNA library.



DNA Sequencing

DNA sequencing is a core activity of genomics research, with the resulting digital sequence facilitating the explosion of discovery we are witnessing currently. DNA sequencing is carried out on samples usually contained within a cloning vector using an enzymatic sequencing reaction much like the PCR amplification reaction, shown in figure 18. The sample DNA is placed in a vector flanked by sequences that pre-made DNA primers recognize. The primers are necessary, because the DNA polymerase enzyme requires some foundation on which to work. The primers hybridize to the DNA adjacent to the sample, and the DNA polymerase then binds to the primers and begins copying the sample template, incorporating nucleotides (individual chemical letters) until one labeled with a dye is incorporated, terminating the individual copying reactions. These copying reactions repeated numerous times, giving rise to many copies of the template, each of varying lengths and ending with a labeled nucleotide corresponding to the letter at which the reaction stopped. The reaction is stopped after sufficient time to yield fragments that span the entire length of the sample, with a label at each letter in the sequence. These then are placed in a DNA sequencer, which separates the fragments based on size, elucidating the sequence of the stretch of DNA. The use of standardized flanking regions and sequencing primers allows researchers to determine what part of a sequence is related to the sample under study and what portion is part of the vector, thus ensuring sequence quality.

