Filed Pursuant to Rule 424(b)(4)
Registration No.333-108202

PROSPECTUS SUPPLEMENT
(To prospectus dated October 2, 2003)

3,988,500 Ordinary Shares

FLAMEL TECHNOLOGIES

Ordinary Shares in the Form of American Depositary Shares

Flamel Technologies S.A. will issue 2,000,000 new ordinary shares and shareholders of Flamel Technologies S.A. are selling 1,988,500 ordinary shares. Each ordinary share will be represented by one American Depositary Share ("ADS").

The ADSs are quoted on the Nasdaq National Market under the symbol "FLML". On October 2, 2003, the last sale price of the ADSs as reported on the Nasdaq National Market was $33.78 per ADS.

Investing in the ADSs involves risks that are described in the "Risk Factors" section beginning on page S-10 of this prospectus supplement.

	Per ADS	Total
Public offering price	$33.25	$132,617,625
Underwriting discount	$1.995	$7,957,058
Proceeds, before expenses, to Flamel Technologies	$31.255	$62,510,000
Proceeds, before expenses, to selling shareholders	$31.255	$62,150,568

The underwriters may also purchase up to an additional 588,000 ordinary shares from the selling shareholders and from an executive officer of Flamel at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement to cover overallotments.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The ADSs will be ready for delivery on or about October 8, 2003.

Merrill Lynch & Co.

UBS Investment Bank
SG Cowen
Punk, Ziegel & Company
Merriman Curhan Ford & Co.
Brean Murray & Co., Inc.

The date of this prospectus supplement is October 2, 2003.

TABLE OF CONTENTS

Prospectus Supplement

Prospectus

In this prospectus supplement, "Flamel," "our company," "we," "us" and "our" refer to Flamel Technologies, and "$" and "dollar" refer to the lawful currency of the United States.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates.

The following product or technology designations are trademarks of Flamel: Asacard™, Agsome™, Genvir™, Basulin®, Micropump®, Medusa® and ColCys®. All other trademarks appearing in this prospectus supplement and the accompanying prospectus are owned by third parties.

This prospectus supplement and the accompanying prospectus are not being distributed in the context of a public offer in France within the meaning of Article L. 411-1 of the French Monetary and Financial Code (*Code monétaire et financier*), and thus this prospectus supplement and the accompanying prospectus have not been and will not be submitted to the *Commission des Opérations de Bourse* for approval in France.

Each of the underwriters has represented and agreed that it has not offered or sold, and will not offer or sell, directly or indirectly, any ADSs to the public in France and has not distributed or caused to be distributed and will not distribute or cause to be distributed to the public in France this prospectus supplement or the accompanying prospectus or any other offering material relating to this offering of ADSs and that such offers, sales and distributions have been and will be made in France only (a) to qualified investors *(investissuers qualifiés*) and/or (b) to a restricted groups of investors (*cercle restreint d'investisseurs*), in each case, acting for their own account, all as defined in, and in accordance with, Articles L. 411-1 and L. 411-2 of the French Monetary and Financial Code and Decree no. 98-880 dated October 1, 1998.

The prospectus supplement and the accompanying prospectus are not to be further distributed or reproduced (in whole or in part) in France by the recipients thereof and this prospectus supplement and the accompanying prospectus have been distributed on the understanding that such recipients will only participate in the issue or sale of the ADSs for their own account and undertake not to transfer, directly or indirectly, the ADSs to the public in France, other than in compliance with all applicable laws and regulations and in particular with Articles L. 411-1 and L. 411-2 of the French Monetary and Financial Code.

PROSPECTUS SUPPLEMENT SUMMARY

Flamel Technologies S.A.

Flamel Technologies S.A. is a biopharmaceutical company principally engaged in the development of proprietary formulations of drug candidates through the application of two patented drug delivery technologies to currently marketed products. Our Medusa® drug delivery technology is designed to provide the controlled-release of therapeutic proteins and peptides. Our Micropump® technology is a controlled-release technology for orally-administered small molecule pharmaceuticals We have fifteen programs in clinical development and six developmental commercial partnerships with leading biopharmaceutical companies.

Our core expertise is in the identification and early stage development of a broad array of clinically and commercially relevant compounds that could significantly be improved through our drug delivery systems. After we establish the pre-clinical feasibility of our compound formulations, we seek to leverage the infrastructure and financial resources of leading biopharmaceutical partners through strategic partnerships. This strategy has enabled us to establish a significant pipeline of clinical candidates with a modest financial resource commitment. We also develop formulations of drugs that are brought to us by the innovators of those drugs.

Our lead product utilizing the Medusa controlled-release technology is Basulin®, a long-acting insulin in phase II trials for the treatment of diabetes. We recently licensed Basulin to Bristol-Myers Squibb Company. We estimate that the long-acting basal insulin market had worldwide sales in 2002 of $2.3 billion. We have a number of other proprietary development programs aimed at improving the clinical performance of known protein therapeutics via the Medusa technology.

Genvir™, our lead product using our Micropump technology, is a controlled-release formulation of acyclovir for the treatment of herpes. The worldwide sales for therapeutic agents for herpes were estimated to be $1.7 billion in 2002. We have licensed Genvir, which has completed one phase III clinical trial and is slated to begin further phase III trials, to Biovail Corporation. We have four additional pharmaceutical development programs utilizing Micropump technology with disclosed partners, including GlaxoSmithKline plc, Merck & Co., Inc. and Servier S.A. In addition, we have a number of drug development programs utilizing Micropump technology that are either licensed to undisclosed partners or still owned entirely by us.

Medusa: Controlled-release Drug Delivery Technology for Therapeutic Proteins

The worldwide market for currently approved protein and peptide drugs is more than $20 billion annually and is expected to grow significantly. New protein drugs are in active development. Despite the significant market, the use of proteins has been limited by certain dosing and formulation difficulties. As most proteins are rapidly metabolized, their clinical benefit has been limited by the ability to deliver these drugs at therapeutic levels over optimal periods of time and with minima variability. The scientific challenges to developing controlled-release processes for protein-based drugs are significant. Successful drug delivery requires a system that:

- can be metabolized by the human body into harmless substances;
- is compatible with the protein or peptide;
- keeps the structure of the protein intact;
- protects the therapeutic agent during transit and delivery; and
- has the required release properties once delivered.

Medusa addresses these needs by delivering controlled levels of proteins over days or weeks. We create nano-scale particles comprised of two amino acids: poly-leucine and poly-glutamate. These polyamino acids self-assemble in water, and therapeutic proteins are attracted to the polymers in water. These particles are often referred to as “depots.” When injected under the skin, the therapeutic proteins are released from the

depots over time at a controlled rate. The speed of release depends on the way the polyamino acid chain is constructed. After releasing the therapeutic proteins, the depot breaks down into the two amino acids, the building blocks of protein, and are used by or excreted from the body. As compared to other long-acting protein formulation technologies such as pegylation and encapsulation, Medusa does not alter the chemical or physical structure of the protein. We believe that by preserving the chemical and structural characteristics of the therapeutic protein, Medusa increases the efficacy of the proteins relative to other technologies.

Basulin: Long-acting Basal Human Insulin Formulation

The most advanced application of our Medusa technology is a depot delivery formulation of insulin targeted to meet the baseline insulin requirements of diabetic patients. Insulin serves to regulate the glucose level in the blood. To maintain control over their glucose levels, insulin-dependent diabetics require two different types of insulin: a fast-acting insulin to be taken at meal times, and a long-acting insulin to maintain a constant minimum level of insulin. The worldwide market for insulin in 2002 exceeded $4.5 billion. Of this total, long-acting basal insulin constituted approximately 50% of this market in annual sales. In head-to-head clinical trials, the effectiveness of Basulin was at least equivalent to Aventis' Lantus, the current market leader.

Other Products Based on the Medusa System

We believe that the Medusa delivery system has the potential to improve formulations of other important biological drugs resulting in more favorable dosing regimens, improved efficacy and reduced side effects. We are developing Medusa formulations for other therapeutic proteins, including erythropoetin, interferon alpha, human growth hormone and interleukin-2. Moreover, we are conducting feasibility studies for several additional candidates.

Micropump: Controlled-release Drug Delivery Technology for Orally-Administered Drugs

Our other drug delivery platform, Micropump, is a controlled-release technology for orally-administered drugs that provides sustained release and tastemasking enhancements to pharmaceutical formulations. Micropump technology is based on encapsulation of microscopic-sized granulates of a pharmaceutical compound with carefully selected polymers designed to control the absorption rate of the drug. Micropump is designed particularly to improve the dosing of pharmaceuticals that are absorbed primarily in the small intestine, which constitute a significant percentage of orally-administered pharmaceuticals.

Micropump technology has several potential advantages when compared to other drug delivery technologies that prolong the delivery of drug compounds to the small intestine, including gastro-retentive technologies, which are generally comprised of large pills that slowly release the drug from the stomach. Unlike large, difficult to swallow gastro-retentive pills, the Micropump technology can be delivered in conventional size tablets or capsules, as well as in suspensions and syrups for children and sachets (powder). Since the polymers do not interact with the active ingredients, Micropump technology may also facilitate multi-drug combination products. Lastly, Micropump formulations are encapsulated, minimizing potential stomach irritation from the active ingredient.

Genvir: Controlled-Release Oral Acyclovir

We have applied Micropump technology to develop Genvir, a controlled-release formulation of acyclovir for the treatment of herpes. The annual market for treatment of herpes is approximately $1.7 billion. Acyclovir is currently the leading drug for the treatment of herpes infections; however, it has an arduous dosing regimen, up to five times a day. Two second-generation acyclovir-derived products, GlaxoSmithKline's Valtrex® (valacyclovir) and Novartis's Famvir® (famciclovir), have improved dosing to twice a day. Genvir is an oral drug with a dosing schedule equivalent to Valtrex and Famvir. Phase III clinical results to date have indicated that Genvir is bioequivalent to currently marketed five times-a-day acyclovir products.

Other Products Based on Micropump Technology

We have two other proprietary pharmaceutical formulations that we have developed, Asacard™ and Metformin XL. We also have Micropump formulation projects partnered with Servier, Merck, GlaxoSmithKline and several other undisclosed pharmaceutical companies. In addition we are conducting feasibility studies for several additional candidates.

Medusa and Micropump Products

Product Candidate	Indication	Status	Partner
Medusa			
Basulin	Diabetes	Phase II	Bristol-Myers Squibb
Interleukin-2	Cancer	Pre-clinical	In-house
Erythropoetin (EPO)	Anemia	Pre-clinical	In-house
Interferonα	Hepatitis C, cancer	Pre-clinical	In-house
Human growth hormone	Short stature	Pre-clinical	In-house
Other feasibility study agreements	Multiple	Pre-clinical	Undisclosed
Micropump			
Genvir	Herpes	Phase III	Biovail (U.S. and Canada)
Metformin XL	Diabetes	Phase II	In discussions
ACE Inhibitor	Cardiovascular disease	Confidential	Servier
Project A	Undisclosed	Confidential	Merck
Augmentin SR	Infectious diseases	Confidential	GlaxoSmithKline
Undisclosed drug	NA	Confidential	GlaxoSmithKline
Asacard (aspirin)	Cardiovascular disease	Approved 11 Countries (Europe)	In discussions
Other feasibility study agreements	Multiple	Confidential	Multiple

Business Strategy

We aim to build on our core strength as a science-based, market-focused innovator of controlled-release drug delivery systems. The key elements of our strategy that should enable us to build upon our strengths are as follows:

- maximize the potential of our existing drug delivery systems;
- develop or acquire additional drug delivery technologies:
  - by identifying additional compounds for unmet medical needs;
  - by developing new formulations of proprietary compounds that we receive from additional collaborators; and
- leverage capabilities of pharmaceutical partners for clinical development and commercialization.

We believe that we have a competitive advantage in developing controlled-release formulations of proteins, peptides and small molecules that improve dosing, compliance and efficacy. We remain committed to focusing on our strengths. We will continue to partner our proprietary formulations with pharmaceutical companies with the clinical, regulatory and marketing resources to secure regulatory approval and to commercialize these pharmaceuticals successfully.

Under our partnering agreements, our pharmaceutical company partners typically assume responsibility for all clinical, regulatory and marketing costs and make payments to us at the time the agreement is signed and upon the achievement of significant technical, clinical and regulatory milestones. We also typically are entitled to receive ongoing royalty payments on the sales of pharmaceuticals that incorporate our technologies.

Recent Developments

On August 27, 2003, we announced that we licensed our controlled-release long-acting human insulin product, Basulin, to Bristol-Myers Squibb. The licensing agreement, which is subject to antitrust clearance, provides for an initial payment to us of $20 million, additional milestone payments that could reach $145 million and double-digit royalties on the sale of the product. Bristol-Myers Squibb also has assumed all future development, registration and marketing costs of the product in exchange for worldwide marketing rights.

On June 19, 2003, we announced the election of three new directors to our board of directors. The three new directors are Raul Cesan, former president and chie operating officer of Schering Plough Corporation and a current director of The New York Times Company; William Dearstyne, former company group chairman of Johnson & Johnson; and Michel Greco, formerly directeur général délégué and member of the board of directors of Aventis Pasteur.

On April 9, 2003, we announced that we licensed Genvir, our controlled-release formulation of acyclovir for the treatment of genital herpes, to Biovail for the U.S. and Canadian markets. We retained the rights to the product in the rest of the world.

On March 28, 2003, we announced our second Micropump technology license agreement with GlaxoSmithKline for an undisclosed product. The terms of the license agreement include $25 million in milestone payments and royalties on sales of the product. We and GlaxoSmithKline estimate that royalties in the first year following launch of sales of the product could range up to $20 million, assuming continued successful development and commercialization of the product.

*** ***

Our principal executive offices are located at 33 Avenue du Docteur Georges Levy, 69693 Vénissieux Cedex, France, and our telephone number is 011 (33) 4 72 78 34 34. The address of our Washington, D.C. office is 2121 K Street N.W., Suite 650, Washington, D.C. 20037, and our telephone number at this address is (202) 862-8400.

The Offering

Ordinary shares offered:	
By Flamel Technologies through Merrill, Lynch, Pierce, Fenner & Smith	2,000,000 new shares
By the selling shareholders	1,988,500 shares
Total	3,988,500 shares
Ordinary shares outstanding after the offering	21,291,590 shares
The ADSs	The ordinary shares are being offered in the form of ADSs. Each ADS represents one ordinary share.
Use of proceeds	We estimate that our net proceeds from the issuance of the 2,000,000 new ordinary shares will be approximately $62.1 million. We intend to use these net proceeds for: • research and development; and • working capital and general corporate purposes. We will not receive any proceeds from the sale of ordinary shares by the selling shareholders, including the over-allotment option shares, if any.
Risk factors	See “Risk Factors” and other information contained or incorporated by reference in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our ADSs.
Nasdaq National Market symbol	FLML

The number of ordinary shares outstanding after the offering excludes (1) 3,092,500 ordinary shares reserved for issuance under our stock option plans, of which options to purchase 2,565,000 ordinary shares at an average option price of €3.66 ($4.17) have been issued, (2) 995,000 ordinary shares underlying currently unexercised warrants and (3) warrants reserved for certain directors to purchase 200,000 ordinary shares at an exercise price of €9.88 proposed by our Board of Directors on June 13, 2003 for approval by our shareholders at the next extraordinary meeting of shareholders.

SUMMARY CONSOLIDATED FINANCIAL DATA

The summary consolidated financial data for each of the five years in the period ended December 31, 2002 are derived from the consolidated financial statements of Flamel, which have been prepared in accordance with U.S. GAAP and audited by Ernst & Young Audit, independent auditors. The data as of and for the six months ended June 30, 2003 and 2002 have been derived from unaudited interim financial statements of Flamel, which, in the opinion of Flamel's management, include all normal and recurring adjustments that are considered necessary for the fair presentation of the results for the interim period. The historical results set forth below and elsewhere in this document are not indicative of the future performance of Flamel, and the interim results set forth below are not necessarily indicative of the operating results for the full year. You should read the summary consolidated financial data of Flamel set forth below in conjunction with the consolidated financial statements and the notes related thereto included in this prospectus supplement or incorporated herein by reference.

	Year Ended December 31,					For the Six Months Ended June 30, (Unaudited)	
	1998	1999	2000	2001	2002	2002	2003
	(in thousands, except per share data)						
Statements of Operations Data:							
Revenues	$ 9,522	$ 11,040	$ 10,902	$ 13,087	$ 18,406	$ 7,209	$ 8,532
Costs and expenses	(18,813)	(18,040)	(16,107)	(16,242)	(18,629)	(8,577)	(12,691)
Loss from operations	(9,291)	(7,000)	(5,205)	(3,155)	(223)	(1,368)	(4,159)
Interest and other expense, net	232	322	371	295	149	69	(151)
Other income	—	—	—	—	2,526(1)	2,396(1)	1,007(2)
Income (loss) before income tax and the cumulative effect of a change in accounting principle	(9,059)	(6,678)	(4,834)	(2,860)	2,452	959	(3,303)
Income tax benefit (charge)	1,247	(16)	(50)	(14)	553	—	(21)
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition	—	—	(4,577)	—	—	—	—
Net income (loss)	$ (7,812)	$ (6,694)	$ (9,461)	$ (2,874)	$ 3,005	$ 959	$ (3,324)
Earnings (loss) per share before cumulative effect of change in accounting principle	$ (0.65)	$ (0.52)	$ (0.32)	$ (0.18)	$ 0.19	$ 0.06	$ (0.20)
Basic earnings (loss) per ordinary share	$ (0.65)	$ (0.52)	$ (0.62)	$ (0.18)	$ 0.19	$ 0.06	$ (0.20)
Diluted earnings (loss) per share	$ (0.65)	$ (0.52)	$ (0.62)	$ (0.18)	$ 0.18	$ 0.06	$ (0.20)
Basic weighted average number of shares outstanding	12,046	12,939	15,331	16,198	16,198	16,198	16,327
Diluted weighted average number of shares outstanding	12,046	12,939	15,331	16,198	16,711	16,711	16,327
Dividends per share	—	—	—	—	—	—	—

	At December 31,					At June 30,	
	1998	1999	2000	2001	2002	2002	2003
				(in thousands)			
Balance Sheet Data:							
Cash and cash equivalents	$ 7,277	$ 5,210	$10,137	$ 5,309	$14,527	$11,906	$11,649
Total assets	25,318	14,920	20,360	18,144	23,076	19,634	23,856
Total long-term liabilities(3)	3,180	2,358	3,365	4,174	4,281	4,238	5,419
Shareholders' equity	17,785	9,067	10,882	7,509	12,286	9,570	10,641

(1) Other income consists principally of the amount received from the Wellcome Foundation in settlement of certain litigation with respect to Genvir in January 2002.

(2) In February 2003, we recognized other income of $376,000 from the sale of equipment in our Vénissieux pilot plant. In March 2003, we recognized other income of $768,000 from grants made by French public agencies linked to investments in the development of our pharmaceutical production facility located in Pessac, France, following the achievement of the conditions of those grants.

(3) Includes deferred revenues, less current portion, of $0 million, $0 million, $1.6 million, $2.9 million and $2.0 million at December 31, 1998, 1999, 2000, 2001 and 2002, respectively, and of $2.7 million and $2.7 million at June 30, 2002 and 2003, respectively.

RISK FACTORS

This prospectus supplement contains forward-looking statements based on our current expectations. You should be aware that these statements are projections or estimates as to future events, and actual results may differ materially. You should carefully consider the following risk factors, in addition to the other information contained in this prospectus supplement and in any other documents to which we refer you in this prospectus supplement, before purchasing our securities. The risks and uncertainties described below are not the only ones we face.

We depend on a few customers for the majority of our revenues, and the loss of any one of these customers could reduce our revenues significantly.

We depend on a few customers and partners for the majority of our revenues, including Bristol-Myers Squibb Company, GlaxoSmithKline, Merck & Co., Inc., Servier and Biovail. The termination of our relationship with any of these major customers or partners, and our failure to broaden our customer base, could cause our revenues to decrease significantly and result in losses from our operations. Further, we may be unable to negotiate favorable business terms with customers that represent a significant portion of our revenues. If so, our revenues and gross profits, if any, may not grow as expected or may not grow at a rate sufficient to allow us to achieve profitability.

Our revenues depend on pharmaceutical and biotechnology companies successfully developing products that incorporate our drug delivery technologies.

We market and sell our technologies to third parties, who incorporate our technologies into their products. We depend upon collaborative agreements with pharmaceutical and biotechnology companies to develop, test, obtain regulatory approval for and commercialize products that incorporate our drug delivery technologies. We currently have collaborative agreements with Bristol-Myers, Servier, GlaxoSmithKline, Merck, Corning Incorporated and a number of other pharmaceutical and biotechnology companies.

The number of products that our partners successfully develop under these collaborative agreements will affect our revenues. We cannot control the timing and other aspects of the development or marketing by our pharmaceutical and biotechnology company partners of their products that incorporate our technologies. The failure of one or more of our partners to develop successful products that incorporate our technologies or to perform as we expect under our agreements with them could have a material and adverse impact on our revenues and profits. We face risks relating to our collaborative agreements, including risks that:

- our collaborative agreements may not result in any new commercial products;
- the existing commercial products developed under our collaborative agreements may not be successful;
- our pharmaceutical and biotechnology company partners may not successfully market any commercial products;
- we may not be able to meet the milestones established in our current or future collaborative agreements;
- we may not be able to successfully develop new drug delivery technologies that would be attractive to potential pharmaceutical or biotechnology company partners; and
- our collaborative partners may terminate their relationships with us.

Although products that incorporate our drug delivery technologies may appear promising at their early stages of development and in clinical trials, none of these potential products may reach the commercial market for a number of reasons.

Successful research and development of pharmaceutical products is difficult and expensive and many product candidates fail to reach the market. Accordingly, it is possible that products that incorporate our technologies may never reach the commercial market for any number of reasons. We intend to continue to

enhance our current technologies and pursue additional proprietary drug delivery technologies. Our success will depend on the discovery and the successful commercialization of products that can utilize our drug delivery technologies. If products using our technologies fail to reach the commercial market, our revenues would be adversely affected, and we may be unable to increase our revenue.

Even if our technologies appear promising during various stages of development, there may not be successful commercial applications developed for them because:

- they may be found to be ineffective or cause harmful side effects, or they may fail during pre-clinical testing or clinical trials;
- we may not find pharmaceutical or biotechnology companies to adopt the technologies;
- our pharmaceutical and biotechnology company partners may find that certain products cannot be manufactured on a commercial scale and, therefore, may not be economical to produce; or
- products that use our technologies also could fail to achieve market acceptance or be precluded from commercialization by proprietary rights of third parties.

We depend on key personnel to execute our business plan. If we cannot attract and retain key personnel, we may not be able to successfully implement our business plan.

Our success depends in large part upon our ability to attract and retain highly qualified personnel. During our operating history, we have assigned many key responsibilities within our company to a relatively small number of individuals, each of whom has played key roles in executing various important components of our business. We do not have employment agreements with any of our key personnel, nor do we maintain material key person life insurance for any of our key personnel. If we lose the services of Dr. Gerard Soula, our Chief Executive Officer, Stephen Willard, our Chief Financial Officer and General Counsel, or Raphael Jorda, our Director of Manufacturing, we may have difficulty executing our business plan in the manner we currently anticipate. Further, because each of our key personnel plays more than one role in respect of numerous components of our business, the loss of any one or more of such individuals could have an adverse effect on our business.

Products that incorporate our drug delivery technologies are subject to regulatory approval. If our pharmaceutical and biotechnology company partners do not obtain such approvals, or if such approvals are delayed, our revenues may be adversely affected.

In the United States, the federal government, principally the U.S. Food and Drug Administration (FDA), and state and local government agencies regulate all pharmaceutical products, including existing products and those under development. Our pharmaceutical and biotechnology company partners may experience significant delays in expected product releases while attempting to obtain regulatory approval for products incorporating our technologies. If they are not successful, our revenues and profitability may decline. We cannot control, and our pharmaceutical and biotechnology company partners cannot control, the timing of regulatory approval for any of these products.

Applicants for FDA approval often must submit extensive clinical and pre-clinical data as well as information about product manufacturing processes and facilities and other supporting information to the FDA. Varying interpretations of the data obtained from pre-clinical and clinical testing could delay, limit or prevent regulatory approval of a drug product. Changes in FDA approval policy during the development period, or changes in regulatory review for each submitted new product application, also may delay an approval or rejection of an application. The FDA has substantial discretion in the approval process and may disagree with our or our partners' interpretations of such data and information which also could cause delays of an approval or rejection of an application. Even if the FDA approves a product, the approval may limit the uses or indications for which a product may be marketed, or may require further studies. The FDA also can withdraw product clearances and approvals for failure to comply with regulatory requirements or if problems follow initial marketing.

The FDA's statutes, regulations or policies may change and additional government regulations or statutes may be enacted which could prevent or delay regulatory approval of biological and other drugs or medical devices. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the U.S. or abroad.

Manufacturers of drugs also must comply with applicable Good Manufacturing Practices (GMP) requirements. If we or our pharmaceutical and biotechnology company partners cannot comply with these practices, the sale of our products or products developed by our partners that incorporate our technologies may be suspended. This would reduce our revenues and gross profits. We may not be able to comply with all of the applicable good manufacturing practices and other FDA regulatory requirements for manufacturing.

If our products or products that incorporate our technologies are marketed in other jurisdictions, we and the partners with whom we are developing our technologies must obtain required regulatory approvals from foreign regulatory agencies and comply with extensive regulations regarding safety and quality. If approvals to market our products are delayed, if we fail to receive these approvals or if we lose previously received approvals, our revenues would be reduced. We may be required to incur significant costs in obtaining or maintaining foreign regulatory approvals.

We may face product liability claims related to participation in clinical trials or the use or misuse of our products or products that incorporate our technologies.

The testing, manufacturing and marketing of our products or products that incorporate our drug delivery technologies may expose us to potential product liability and other claims resulting from their use. If any such claims against us are successful, we may be required to make significant compensation payments. Any indemnification that we have obtained, or may obtain, from contract research organizations or pharmaceutical and biotechnology companies conducting human clinical trials on our behalf may not protect us from product liability claims or from the costs of related litigation. Similarly, any indemnification we have obtained, or may obtain, from pharmaceutical and biotechnology companies with whom we are developing our drug delivery technologies may not protect us from product liability claims from the consumers of those products or from the costs of related litigation. If we are subject to a product liability claim, our product liability insurance may not reimburse us, or be sufficient to reimburse us, for any expenses or losses we may suffer. A successful product liability claim against us, if not covered by, or if in excess of, our product liability insurance, may require us to make significant compensation payments. These payments would be reflected as expenses on our statement of operations and reduce our earnings.

Our commercial products are subject to continuing regulation and we may be subject to adverse consequences if we fail to comply with applicable regulations.

Even if our products receive regulatory approval, either in the United States or internationally, we will continue to be subject to extensive regulatory requirements. These regulations are wide-ranging and govern, among other things:

- adverse drug experience and other reporting regulations;
- product promotion;
- product manufacturing, including good manufacturing practice requirements;
- record keeping requirements;
- drug sampling and distribution requirements;
- electronic record and signature requirements; and
- product manufacturing and labeling changes or modifications.

If we fail to comply with these laws and regulations, we may be fined or barred from selling our products. If the FDA determines that we are not complying with the law, it can:

- issue warning letters;
- impose fines;
- seize products or order recalls;
- issue injunctions to stop future sales of products;
- refuse to permit products to be imported into, or exported out of, the United States;
- suspend or limit our production;
- withdraw previously approved marketing applications; and
- initiate criminal prosecutions.

If our competitors develop and market drug delivery technologies or related products that are more effective than ours, or obtain regulatory approval and market such technology or products before we do, our commercial opportunity will be reduced or eliminated.

Competition in the pharmaceutical and biotechnology industry is intense and is expected to increase. We compete with academic laboratories, research institutions, universities, joint ventures, and other pharmaceutical and biotechnology companies, including other companies developing drug delivery systems. Our Medusa technology competes with technologies from companies such as Alkermes, Inc., SkyePharma plc and Enzon Pharmaceuticals, Inc. Companies with oral drug delivery technology that can compete with our Micropump technology include Eurand International S.p.A., Biovail and Andrx Corporation. We also compete generally with other drug delivery, biotechnology and pharmaceutical and biotechnology companies that develop alternative drug delivery technologies or new drug research and testing.

Many of these competitors have substantially greater financial, technological, manufacturing, marketing, managerial and research and development resources and experience than we do. Furthermore, acquisitions of competing drug delivery companies by large pharmaceutical companies could enhance our competitors' resources. Accordingly, our competitors may succeed in developing competing technologies and products, obtaining regulatory approval and gaining market share for these products more rapidly than we do.

Additionally, there could be new chemical entities that are being developed that, if successful, could compete against our technologies or products. Among the many experimental therapies being tested in the United States and in Europe, there may be some that we do not now know of that may compete with our drug delivery systems or products in the future. These chemical entities and new products may turn out to be safer or may work better than our technologies or products. Our collaborators could choose a competing drug delivery system to use with their drugs instead of one of our drug delivery systems.

If we cannot keep pace with the rapid technological change in our industry, we may lose business.

Our success depends, in part, on maintaining a competitive position in the development of products and technologies in a rapidly evolving field. Major technological changes can happen quickly in the biotechnology and pharmaceutical industries. If we cannot maintain competitive products and technologies, our current and potential pharmaceutical and biotechnology company partners may choose to adopt the drug delivery technologies of our competitors. Our competitors may succeed in developing competing technologies or obtaining governmental approval for products before us, and the products of our competitors may gain market acceptance more rapidly than our products. Such rapid technological change, or the development by our competitors of technologically improved or different products, could render our drug delivery systems obsolete or noncompetitive.

Our products and technologies may not gain market acceptance.

The competitive nature of our industry could adversely affect market acceptance of our products or the use of our drug delivery technologies. Even if we and our pharmaceutical and biotechnology company partners obtain the necessary regulatory approval to market our products and products that incorporate our technologies, our products and technologies may not gain market acceptance among physicians, patients, healthcare payers and the medical community. The degree of market acceptance of any product candidate or technology will depend on a number of factors, including:

- the effectiveness of our marketing strategy;
- demonstration of the clinical efficacy and safety of the product or technology;
- no evidence of undesirable side effects which delay or extend trials;
- no regulatory delays or other regulatory actions;
- its cost-effectiveness;
- its potential advantage over alternative treatment methods; and
- the marketing and distribution support it receives.

If any of our products or technologies fail to achieve market acceptance, our ability to generate revenue will be limited, which would have a material adverse effect on our business.

If we cannot adequately protect our technology and proprietary information, we may be unable to sustain a competitive advantage.

Our success depends, in part, on our ability to obtain and enforce patents for our products, processes and technologies and to preserve our trade secrets and other proprietary information. If we cannot do so, our competitors may exploit our innovations and deprive us of the ability to realize revenues and profits from our developments.

Any patent applications we may have made or may make relating to our potential products, processes and technologies may not result in patents being issued. Our current patents may not be valid or enforceable. They may not protect us against competitors that challenge our patents, such as companies that submit drug marketing applications to the FDA that rely, at least in part, on safety and efficacy data from our products or our business partners' products (*e.g.*, abbreviated new drug applications), obtain patents that may have an adverse effect on our ability to conduct business or are able to circumvent our patents. Further, we may not have the necessary financial resources to enforce our patents.

To protect our trade secrets and proprietary technologies and processes, we rely, in part, on confidentiality agreements with our employees, consultants and advisors. These agreements may not provide adequate protection for our trade secrets and other proprietary information in the event of any unauthorized use or disclosure, or if others lawfully develop the information.

Third parties may claim that our technologies, or the products in which they are used, infringe on their rights and we may incur significant costs resolving these claims.

Third parties may claim that the manufacture, use or sale of our drug delivery technologies infringe on their patent rights. If such claims are asserted, we may have to seek licenses, defend infringement actions or challenge the validity of those patents in court. If we cannot obtain required licenses, are found liable for infringement or are not able to have these patents declared invalid, we may be liable for significant monetary damages, encounter significant delays in bringing products to market or be precluded from participating in the manufacture, use or sale of products or methods of drug delivery covered by the patents of others. We may not have identified, or be able to identify in the future, U.S. and foreign patents that pose a risk of potential infringement claims.

We enter into collaborative agreements with pharmaceutical and biotechnology companies to apply our drug delivery technologies to drugs developed by others. Ultimately, we receive license revenues and product development fees, as well as revenues from the sale of products incorporating our technology and royalties. The drugs to which our drug delivery technologies are applied are generally the property of the pharmaceutical and biotechnology companies. Those drugs may be the subject of patents or patent applications and other forms of protection owned by the pharmaceutical and biotechnology companies or third parties. If those patents or other forms of protection expire, are challenged or become ineffective, sales of the drugs by the collaborating pharmaceutical and biotechnology company may be restricted or may cease.

If we or our collaborative partners are required to obtain licenses from third parties, our revenues and royalties on any commercialized products could be reduced.

The development of some of our products may require the use of technology developed by third parties. The extent to which efforts by other researchers have resulted or will result in patents and the extent to which we or our collaborative partners are forced to obtain licenses from others, if available, on commercially reasonable terms is currently unknown. If we or our collaborative partners must obtain licenses from third parties, fees must be paid for such licenses. These fees would reduce the revenues and royalties we may receive on commercialized products that incorporate our technologies.

If we use biological and hazardous materials in a manner that causes injury, we may be liable for significant damages.

Our research and development activities involve the controlled use of potentially harmful biological materials, hazardous materials and chemicals, and are subject to federal, state and local laws and regulations governing the use, storage, handling and disposal of those materials and specified waste products. We cannot completely eliminate the risk of accidental contamination or injury from the use, storage, handling or disposal of these materials. We currently do not maintain insurance coverage for environmental liabilities. If we fail to comply with environmental regulations, we could be subject to criminal sanctions and/or substantial liability for any damages that result, and any such liability could be significant.

Healthcare reform and restrictions on reimbursements may limit our financial returns.

Our ability to successfully commercialize our products and technologies may depend in part on the extent to which the government health administration authorities, private health insurers and other third party payers will reimburse consumers for the cost of these products. Third party payers are increasingly challenging both the need for and the price of novel therapeutic drugs and uncertainty exists as to the reimbursement status of newly approved therapeutics. Adequate third party reimbursement may not be available for our drug products to enable us to maintain price levels sufficient to realize an appropriate return on our investments in research and product development, which could materially and adversely affect our ability to commercialize that particular drug. We cannot predict the effect that changes in the healthcare system, especially cost containment efforts, may have on our business. Any such changes may adversely affect our business.

Because we have a limited operating history, investors in our shares may have difficulty evaluating our prospects.

We recorded the first commercial sales of products using one of our polymer technologies through our partner, Corning, in 1999. We have had no commercial sales to date of products incorporating either our Medusa or Micropump technologies. Accordingly, we have only a limited operating history, which may make it difficult to evaluate our prospects. The difficulty investors may have in evaluating our prospects may cause volatile fluctuations, including decreases, in the market price of our shares as investors react to information about our prospects. Since 1995, we have generated revenues from product development fees and licensing arrangements and royalties. Our business and prospects, therefore, must be evaluated in light of the risks and uncertainties of a company with a limited operating history and, in particular, one in the pharmaceutical industry.

If we do not remain profitable in the future, the value of our shares may fall.

Although we earned an operating profit for the year ended December 31, 2002, we accumulated aggregate net losses from inception of approximately $56.4 million through that date. If we are unable to earn a profit in future periods, the market price of our stock may fall. The costs for research and product development of our drug delivery technologies and general and administrative expenses have been the principal causes of our losses in prior years. Our ability to achieve profitable operations depends on a number of factors, many of which are beyond our direct control. These factors include:

- the demand for our technologies and products;
- the level of product and price competition;
- our ability to develop additional commercial applications for our products;
- our ability to control our costs;
- our ability to broaden our customer base;
- the effectiveness of our marketing strategy; and
- general economic conditions.

We may require additional financing, which may not be available on favorable terms or at all, and which may result in dilution of your equity interest.

We may require additional financing to fund the development and possible acquisition of new drug delivery technologies and to increase our production capacity beyond what is currently anticipated. If we cannot obtain financing when needed, or obtain it on favorable terms, we may be required to curtail our plans to develop and possibly to acquire new drug delivery technologies or limit the expansion of our manufacturing capacity. We also may elect to pursue additional financing at any time to more aggressively pursue development of new drug delivery technologies and expand manufacturing capacity beyond that currently planned.

Other factors that will affect future capital requirements and may require us to seek additional financing include:

- the development and acquisition of new products and technologies;
- the progress of our research and product development programs;
- results of our collaborative efforts with current and potential pharmaceutical and biotechnology company partners; and
- the timing of, and amounts received from, future product sales, product development fees and licensing revenue and royalties.

Our share price has been volatile and may continue to be volatile.

The trading price of our shares has been, and is likely to continue to be, highly volatile. The market value of an investment in our shares may fall sharply at any time due to this volatility. In the year ended December 31, 2002, the closing sale price for our ADSs as reported on the Nasdaq National Market ranged from $4.85 to $1.22. In the year ended December 31, 2001, the closing sale price of our ADSs as reported on the Nasdaq National Market ranged from $7.06 to $0.94. From January 1, 2003 to September 30, 2003, the closing sale price for our ADSs as reported on the Nasdaq National Market ranged from $42.85 to $3.74. The market prices for securities of drug delivery, biotechnology and pharmaceutical companies historically have been highly volatile. Factors that could adversely affect our share price include:

- fluctuations in our operating results;
- announcements of technological collaborations, innovations or new products by us or our competitors;

- governmental regulations;
- developments in patent or other proprietary rights owned by us or others;
- public concern as to the safety of drugs developed by us or others;
- the results of pre-clinical testing and clinical studies or trials by us or our competitors;
- litigation;
- decisions by our pharmaceutical and biotechnology company partners relating to the products incorporating our technologies;
- actions by the FDA in connection with submissions related to the products incorporating our technologies;
- the perception by the market of biotechnology and high technology companies generally; and
- general market conditions.

Our operating results may fluctuate, which may adversely affect our share price.

Fluctuations in our operating results may lead to fluctuations, including declines, in our share price. Our operating results may fluctuate from period to period due to a variety of factors, including:

- demand by consumers for the products we produce;
- new product introductions;
- pharmaceutical and biotechnology company ordering patterns;
- the number of new collaborative agreements into which we enter;
- the number and timing of product development milestones that we achieve under collaborative agreements;
- the level of our development activity conducted for, and at the direction of, pharmaceutical and biotechnology companies under collaborative agreements; and
- the level of our spending on new drug delivery technology development and technology acquisition, and internal product development.

Variations in the timing of our revenue and expenses could also cause significant fluctuations in our operating results from period to period and may result in unanticipated earning shortfalls or losses.

We have broad discretion over the use of proceeds from this offering.

Our business plan is general in nature and is subject to change based upon changing conditions and opportunities. Our management has broad discretion in applying the net proceeds we estimate we will receive from the issuance of our new ordinary shares in this offering. Our management will have broad discretion in using the proceeds from this offering and may allocate the use of the proceeds in ways with which you may disagree. Because we are not required to allocate the net proceeds from this offering to any specific investment or transaction, you cannot determine at this time the value or propriety of our application of the proceeds. Moreover, you will not have the opportunity to evaluate the economic, financial or other information on which we base our decision on how to use our proceeds. We may use the proceeds for corporate purposes that do not immediately enhance our prospects for the future or increase the value of your investment. As a result, you and other shareholders may not agree with our decisions.

SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus supplement, the accompanying prospectus and the documents incorporated herein by reference contain forward-looking statements. We may make additional written or oral forward-looking statements from time to time in filings with the SEC or otherwise. The words "believe," "expect," "anticipate," and "project" and similar expressions identify forward-looking statements, which speak only as of the date the statement is made. Such forward-looking statements are within the meaning of that term in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Although we believe that our expectations are based on reasonable assumptions within the bounds of our knowledge of our business and operations, our business is subject to significant risks and there can be no assurance that actual results of our development and manufacturing activities and our results of operations will not differ materially from our expectations. Factors that could cause actual results to differ from expectations include, among others:

- our product candidates, if approved for marketing, may not produce significant revenues and we rely on our partners to determine the regulatory and marketing strategies;
- our product candidates, in commercial use, may have unintended side effects, adverse reactions or incidents of misuse;
- we may enter into a collaboration with a third party to market or fund a proprietary product candidate and the terms of such a collaboration may not meet our expectations;
- our delivery technologies or product development efforts may not produce safe, effective or commercially viable products;
- our collaborators could elect to terminate or delay programs at any time and disputes with collaborators or failure to negotiate acceptable new collaborative arrangements for our technologies could occur;
- we may be unable to manufacture or, if our products are successful, scale-up the manufacturing of our products economically or on a commercial scale;
- unexpected events could interrupt manufacturing operations at our facilities, which are the sole source of supply for these products;
- after the completion of clinical trials of products incorporating our technologies and the submission to the FDA of a New Drug Application, or NDA, for marketing approval and to other health authorities as a marketing authorization application, the FDA or other health authorities could refuse to accept such filings or could request additional pre-clinical or clinical studies be conducted, each of which could result in significant delays, or such authorities could refuse to approve the product at all;
- our product candidates could be ineffective or unsafe during pre-clinical studies and clinical trials and we and our collaborators may not be permitted by regulatory authorities to undertake new or additional clinical trials for product candidates incorporating our technologies, or clinical trials could be delayed;
- we may experience significant delays in clinical trials on our products;
- we may not realize any revenue from milestone or royalty payments under our license agreements with our partners, including Bristol-Myers;
- even if our product candidates appear promising at an early stage of development, product candidates could fail to receive necessary regulatory approvals, be difficult to manufacture on a large scale, be uneconomical, fail to achieve market acceptance, be precluded from commercialization by proprietary rights of third parties or experience substantial competition in the marketplace;
- technological changes in the biotechnology or pharmaceutical industries could render our product candidates obsolete or noncompetitive;

- we may face difficulties or set-backs in obtaining and enforcing our patents or defending claims of patent infringement by others; and

- we may need to raise substantial additional funding to continue research and development programs and clinical trials and could incur difficulties or setbacks in raising such funds.

Forward-looking statements are subject to inherent risks and uncertainties, some of which cannot be predicted or quantified. Future events and actual results could differ materially from those set forth in, contemplated by or underlying the forward-looking statements. Statements in this prospectus supplement, the accompanying prospectus and documents incorporated by reference, including those set forth in “Risk Factors” in this prospectus supplement, describe factors, among others, that could contribute to or cause such differences.

USE OF PROCEEDS

We estimate that the net proceeds that we will receive from the subscription of the 2,000,000 new shares to be issued will be approximately $62.1 million after deducting underwriting discounts and commissions and our offering expenses. We will not receive any of the proceeds from the sale of the ADSs offered by the selling shareholders.

We expect to use the net proceeds from the subscription of the newly issued shares for research and development, working capital and general corporate purposes, including general and administrative expenses. We also expect the net proceeds from this offering to contribute toward strengthening our financial position. The amounts and timing of our actual expenditures will depend significantly upon a number of factors, including future revenues from licensing and corporate collaborations. As a result, we will retain broad discretion in determining how we will allocate the net proceeds from this offering. Pending these uses, we intend to invest the net proceeds in short-term, interest bearing instruments or other investment-grade corporate and government securities.

PRICE RANGE OF AMERICAN DEPOSITARY SHARES AND DIVIDEND POLICY

Since 1996, our ADSs have been traded on the Nasdaq National Market. We currently trade under the symbol “FLML”. The following table sets forth the high and low reported sales prices for our ADSs for the period indicated as reported on the Nasdaq National Market.

	High	Low
2003		
First Quarter	$ 7.15	$ 3.74
Second Quarter	14.09	7.10
Third Quarter	43.60	12.50
2002		
First Quarter	$ 2.95	$ 1.78
Second Quarter	2.16	1.23
Third Quarter	3.25	1.22
Fourth Quarter	4.85	2.21

On October 2, 2003, the last reported sale price of our ADSs as reported on the Nasdaq National Market was $33.78 per ADS. As of June 30, 2003, we had 25 holders of record of our ADSs.

We have never declared or paid cash dividends on our ADSs. We do not intend to declare or pay any cash dividends on our ADSs in the foreseeable future. We plan to retain any earnings for use in the operation of our business and to fund future growth.

CAPITALIZATION

The table below sets forth the following as of June 30, 2003:

- our historical cash and capitalization; and
- our cash and capitalization as adjusted to give effect to the issuance by us of 2,000,000 ADSs at the public offering price of $33.25 per ADS, after deducting underwriting discounts and commissions and our offering expenses.

Actual ADS data are as of June 30, 2003 and exclude:

- 2,708,000 ordinary shares issuable upon the exercise of options to subscribe or purchase ordinary shares issued under our stock option plans at a weighted average price of €4.01 ($4.57);
- 3,816,500 ordinary shares issuable upon the exercise of warrants exercisable at a price of €3.92 ($4.47); and.
- 527,500 ordinary shares underlying unallocated stock options under previous stock option plans.

This table should be read in conjunction with our consolidated financial statements and notes thereto and "Management's Discussion and Analysis of Financial Condition and Results of Operations" beginning on page S-25.

	As of June 30, 2003	
	Actual	As Adjusted
	(In thousands)	
Cash, cash equivalents and marketable securities	$ 11,649	$ 73,784
Total long-term liabilities	$ 5,419	$ 5,419
Shareholders' equity:		
Ordinary shares; 23,379,090 ordinary shares authorized; 16,327,090 issued and outstanding actual and 18,327,090 issued and outstanding as adjusted	2,384	2,668
Additional paid-in capital	71,854	133,705
Accumulated deficit	(59,704)	(59,704)
Deferred compensation	(10)	(10)
Cumulative other comprehensive loss	(3,883)	(3,883)
Total shareholders' equity	10,641	72,776
Total capitalization	$ 16,060	$ 78,195

SELECTED CONSOLIDATED FINANCIAL DATA

The selected consolidated financial data for each of the five years in the period ended December 31, 2002 are derived from the consolidated financial statements of Flamel, which have been prepared in accordance with U.S. GAAP and audited by Ernst & Young Audit, independent auditors. The data as of and for the six months ended June 30, 2003 and 2002 have been derived from unaudited interim financial statements of Flamel, which, in the opinion of Flamel's management, include all normal and recurring adjustments that are considered necessary for the fair presentation of the results for the interim period. The historical results set forth below and elsewhere in this document are not indicative of the future performance of Flamel, and the interim results set forth below are not necessarily indicative of the operating results for the full year. You should read the summary consolidated financial data of Flamel set forth below in conjunction with the consolidated financial statements and the related notes included in this prospectus supplement or incorporated herein by reference.

	Year Ended December 31,					Six Months Ended June 30, (Unaudited)	
	1998	1999	2000	2001	2002	2002	2003
	(in thousands, except per share data)						
Statements of Operations Data:							
Revenues	$ 9,522	$ 11,040	$ 10,902	$ 13,087	$ 18,406	$ 7,209	$ 8,532
Costs and expenses	(18,813)	(18,040)	(16,107)	(16,242)	(18,629)	(8,577)	(12,691)
Loss from operations	(9,291)	(7,000)	(5,205)	(3,155)	(223)	(1,368)	(4,159)
Interest and other expense, net	232	322	371	295	149	(69)	(151)
Other income	—	—	—	—	2,526 (1)	2,396 (1)	1,007 (2)
Income (loss) before income tax and the cumulative effect of a change in accounting principle	(9,059)	(6,678)	(4,834)	(2,860)	2,452	959	(3,303)
Income tax benefit (charge)	1,247	(16)	(50)	(14)	553	—	(21)
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition	—	—	(4,577)	—	—	—	—
Net income (loss)	$ (7,812)	$ (6,694)	$ (9,461)	$ (2,874)	$ 3,005	$ 959	$ (3,324)
Earnings (loss) per share before cumulative effect of change in accounting principle	$ (0.65)	$ (0.52)	$ (0.32)	$ (0.18)	$ 0.19	$ 0.06	$ (0.20)
Basic earnings (loss) per ordinary share	$ (0.65)	$ (0.52)	$ (0.62)	$ (0.18)	$ 0.19	$ 0.06	$ (0.20)
Diluted earnings (loss) per share	$ (0.65)	$ (0.52)	$ (0.62)	$ (0.18)	$ 0.18	$ 0.06	$ (0.20)
Basic weighted average number of shares outstanding	12,046	12,939	15,331	16,198	16,198	16,198	16,327
Diluted weighted average number of shares outstanding	12,046	12,939	15,331	16,198	16,711	16,711	16,327
Dividends per share	—	—	—	—	—	—	—

	At December 31,					At June 30,	
	1998	1999	2000	2001	2002	2002	2003
				(in thousands)			
Balance Sheet Data:							
Cash and cash equivalents	$ 7,277	$ 5,210	$10,137	$ 5,309	$14,527	$11,906	$11,649
Total assets	25,318	14,920	20,360	18,144	23,076	19,634	23,856
Total long-term liabilities(3)	3,180	2,358	3,365	4,174	4,281	4,238	5,419
Shareholders' equity	17,785	9,067	10,882	7,509	12,286	9,570	10,641

(1) Other income consists principally of the amount received from the Wellcome Foundation in settlement of certain litigation with respect to Genvir in January 2002.

(2) In February 2003, we recognized other income of $376,000 from the sale of equipment in our Vénissieux pilot plant. In March 2003, we recognized other income of $768,000 from grants made by French public agencies linked to investments in the development of our Pessac facility, following the achievement of the conditions of those grants.

(3) Includes deferred revenues, less current portion, of $0 million, $0 million, $1.6 million, $2.9 million and $2.0 million at December 31, 1998, 1999, 2000, 2001 and 2002, respectively, and of $2.7 million and $2.7 million at June 30, 2002 and 2003, respectively.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF

FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following in conjunction with our consolidated financial statements, including the related notes, contained elsewhere in this prospectus supplement. The following discussion also contains forward-looking statements about our plans, objectives and future results. These forward-looking statements are based on our current expectations, and we assume no obligation to update this information. Realization of these plans and results involves risk and uncertainties, and our actual results could differ materially from those discussed here. Factors that could cause or contribute to such differences include those set forth under the heading "Risk Factors."

Overview

We are a biopharmaceutical company principally engaged in the development of two unique polymer based delivery systems for medical applications. Our Medusa nano-particulate technology is designed to deliver therapeutic proteins, peptides and small molecules. Our lead product utilizing the Medusa technology, Basulin, is a long-acting insulin for the treatment of diabetes. Basulin is the first application of this patented delivery system. We recently licensed Basulin to Bristol-Myers. Micropump is a controlled-release technology for the oral administration of small molecules. Genvir, our lead product using our Micropump technology, is a controlled-release formulation of acyclovir for the treatment of genital herpes. We have licensed Genvir to Biovail.

In 2002, and in the first six months of 2003, our internally funded development efforts were focused on the pre-clinical and initial clinical testing of Basulin, and the application of the Medusa system to other important therapeutic proteins. Internal funding of other projects was kept to a minimal level in an effort to conserve cash. Activities related to photochromic technologies were fully funded by collaborative partners. As in previous years, in 2002, a major part of our revenues came from licensing fees and contract research payments paid by corporate partners. Asacard, a controlled-release aspirin, has been approved for sale in the United Kingdom and several other European countries. Our innovative technologies have also been instrumental in the development of a photochromic eyeglass lens product that was launched by Corning in 1999. In 2002, we recognized revenue from receipt of royalty payments related to the sales of Corning's photochromic sunglasses lenses containing technology developed by us. Royalty payments are expected to continue, but will fluctuate according to the success of Corning in commercializing these products.

Our core technologies are focused on improving delivery properties of existing products. We have established long-term development and commercialization partnerships with leading biopharmaceutical companies to maximize the breadth of our technology and leverage the capabilities of our partners.

As in previous years, in 2002 and in the first six months of 2003, a major part of our revenue came from licensing fees and contract research payments received from our biotechnology and pharmaceutical company partners. In recent years, revenue from the sale of products and performance of services included a mix of revenue from a contract manufacturing agreement with GlaxoSmithKline and other major pharmaceutical companies, the sale of photochromic material to Corning, and the performance of various analytical and manufacturing services for other customers. Until our manufacturing capabilities are needed to produce the proprietary products currently in development, we will seek to utilize our manufacturing capacity and to cover our related costs by building a manufacturing services business and by transferring our manufacturing chemical production capability from the Vénissieux pilot plant to the Pessac site.

In the future, we expect that our costs of goods sold may increase as a result of an increase in manufacturing costs. We also expect that research and development may decrease as a percentage of revenues.

In 2002, the majority of our expenses were incurred in Euros. However, a significant portion of our revenues was, and will continue to be, denominated in U.S. dollars. In 2002, 66% of revenues were denominated in U.S. dollars; in 2001, 41% of revenues were denominated in U.S. dollars; and in 2000, 29% of revenues were denominated in U.S. dollars. In each of these years, fluctuations in the value of the Euro relative to the U.S. dollar caused translated amounts to vary from one period to another, affecting our

reported results. Comparisons in financial statement line items between the years ended December 31, 2002 and December 31, 2001 were affected by a 5% average increase in the value of the Euro relative to the U.S. dollar during the year and a 19% increase in the Euro relative to the U.S. dollar at year-end. The conversion of our financial accounts to U.S. dollars is calculated in accordance with the value of the Euro relative to the U.S. dollar. We do not engage in any hedging activities with respect to the risk of exchange rate fluctuations.

We have incurred substantial losses since our inception, and through December 31, 2002, we had an accumulated deficit of approximately $56.4 million. While we earned a profit in the year ended December 31, 2002, we expect to continue our investment and spending in our research and development activities and to maintain our primary facilities and business infrastructure. Thus, we can offer no assurance that we will not incur further losses, at least for the next two years, if our revenue does not sufficiently cover expenditures. As of December 31, 2002, we had approximately $30.4 million in French net operating loss carry-forwards of which approximately $9.4 million have no expiration date. The remaining approximate carry-forwards expire as follows: $7.5 million on December 31, 2003; $5.0 million on December 31, 2004; $6.6 million on December 31, 2005; and $1.9 million on December 31, 2006.

Our business is subject to substantial risks, including the uncertainties associated with the research and development of new products or technologies, the length of time and uncertainty linked to the results of clinical trials and regulatory procedures, uncertainties relating to our collaborative arrangements with large companies, difficulties in the scale-up and manufacturing of our products, and the uncertainty relating to the market acceptance of new products based on our technologies. The time required for us to achieve profitability, and consequently, the amount of future losses, is highly uncertain. Operating losses may also fluctuate from quarter to quarter as a result of differences in timing of revenues recognized or expenses incurred. See “Risk Factors.”

Critical Accounting Policies

The discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements and related notes, which have been prepared in accordance with U.S. GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. We evaluate our estimates, including those related to revenue recognition, accounts receivable, bad debts, inventories, warranty obligations, litigation and deferred tax assets on an on-going basis. We base our estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We believe our more significant judgments and estimates used in the preparation of our consolidated financial statements are made in connection with the following critical accounting policies.

Revenue Recognition

Our significant accounting policies are summarized in Note 1 to our consolidated financial statements. From time to time we receive advance payments from strategic partners, usually at the beginning of our alliance with that partner. As described in Note 1.4 to our consolidated financial statements, these advance payments are recorded as deferred revenue and are recognized on a “systematic and rational basis” to match the revenues with the related costs. Our practice, which we expect to continue in the future, has been to recognize these amounts over the term of the related product development period with respect to which the contract pertains. Other than the foregoing, management does not believe that the application of any of these accounting policies requires material estimates or assumptions on its part.

Results of Operations

Six Months ended June 30, 2003

Revenues for the six months ended June 30, 2003 increased to $8.5 million, compared to $7.2 million for the first half of 2002.

License and research revenue for the six months ended June 30, 2003 of $6.3 million included $2.7 million revenue from GlaxoSmithKline, $2.0 million from Servier, $1.0 million from feasibility studies with other partners and $192,000 from the ongoing research collaboration with Corning. License and research revenue for the first half of 2002 largely consisted of revenues from Novo Nordisk A/S, Corning and various undisclosed partners.

Other revenues for the six months ended June 30, 2003 consisted of royalties from Corning. Other income included $768,000 in French government grants. Other income in the first quarter of 2002 included approximately $2.3 million received in settlement of litigation with the Wellcome Foundation regarding our long-acting acyclovir product Genvir. Revenues from product sales and services were $1.9 million in the six months ended June 30, 2003, compared to $1.3 million in the first six months of 2002, largely as a result of increased contract manufacturing.

Total operating costs for the six months ended June 30, 2003 amounted to $12.7 million, up from $8.6 million in the comparable half of 2002, largely as a result of the increased value of the Euro to the dollar and increases in clinical and pre-clinical studies. Research and development costs for the first six months of 2003 increased to $8.5 million from $5.7 million in the first half of 2002, largely as a result of the exchange rate and clinical and pre-clinical trial expenses. Sales, general and administrative costs increased to $2.4 million from $1.8 million in the first half of 2002, largely due to variation in exchange rates.

Overall, we had a net loss of $3.3 million for the six months ended June 30, 2003, or about $0.20 per share on a diluted basis, compared to a net gain of $1.0 million, or $0.06 per share on a diluted basis, in the comparable period in 2002.

As a result of fluctuations in the amount of quarterly revenues, which may arise from the signing of research collaborations, license agreements or other extraordinary transactions, interim results are not necessarily indicative of the operating results for the full year.

Years ended December 31, 2002, 2001 and 2000

Operating Revenues

We had total revenues of $18.4 million in 2002, $13.1 million in 2001 and $10.9 million in 2000.

In 2002, license and research payments from our various partners totaled $14.6 million. Similar license and research payments in 2001 and 2000 totaled $9.9 million and $6.6 million, respectively. License revenues in 2002 consisted primarily of $6.5 million from Servier and $1.7 million from GlaxoSmithKline. License revenues in 2001 included $2.8 million from Novo Nordisk, which represented the last portion of the $5.0 million up-front fee received in year 1999, which was fully recognized in 2001 due to the termination of the license agreement with Novo Nordisk. License revenues in 2000 included $1.6 million from Novo Nordisk, which represented a portion of the $5.0 million up-front fee received in 1999, but recognized in 2000 due to a change in accounting principle concerning revenue recognition of up front payments. License revenues in 2000 also included a $500,000 fee from Searle for the contract concerning our Asacard product, and license revenues in 1999 included the $5.0 million fee from Novo Nordisk in conjunction with the signing of a development and licensing agreement regarding Basulin, our long-acting insulin product.

In 2002, product sales and services revenues totaled $2.9 million and included $121,000 from GlaxoSmithKline for the manufacture of cimetidine, $539,000 from Corning for replenishment of inventories of photochromic material and $2.2 million from clinical batches and contract manufacturing with various customers. In 2001, product sales and services revenues totaled $2.0 million and included $300,000 from GlaxoSmithKline for the manufacture of cimetidine and $1.4 million from Corning for replenishment of

inventories of photochromic material. In 2000, product sales and services revenues totaled $3.0 million and included $1.2 million from GlaxoSmithKline for the manufacture of cimetidine and $1.4 million from Corning for replenishment of inventories of photochromic material.

Other revenues of $948,000 in 2002 consisted primarily of royalties from Corning related to the sales of photochromic lenses incorporating our technology. Other revenues of $1.2 million in 2001 included $961,000 in royalties from Corning related to the sales of photochromic lenses incorporating our technology, and $219,000 related to the forgiveness of a French government agency loan. Other revenues of $1.2 million in 2000 included $1.1 million in royalties from Corning related to sales of photochromic lenses incorporating our technology, and $115,000 related to the forgiveness of a French government agency loan.

Operating Expenses

We had total costs and expenses of $18.6 million in 2002, $16.2 million in 2001, and $16.1 million in 2000.

Research and development costs represent our most significant operating expenses. These totaled $12.2 million in 2002, $10.7 million in 2001 and $9.8 million in 2000. In 2002, research and development costs increased by approximately $1.5 million over 2001. This increase was primarily due to the increase in the value of the Euro, the currency in which these expenses were paid, against the U.S. dollar. In 2001, research and development costs increased by approximately $900,000 over 2000. This increase was due to a number of new partnerships obtained during the year and to the active pursuit of self-funded programs.

Costs of goods and services sold were $2.4 million in 2002, $2.2 million in 2001 and $2.9 million in 2000. These costs include the direct and indirect labor, materials, outside services, overhead costs relevant to manufacturing and other services provided to third parties at the Pessac facility and at our Vénissieux pilot plant. The fluctuation in costs year-to-year was the result of changes year-to-year in both the mix and volume of products produced and services rendered. The figures show an increase of 10% in 2002 compared to a decline of 24% in 2001.

Selling, general and administrative expenses increased to $4.0 million in 2002 from $3.4 million in 2001 and $3.4 million in 2000. These increases were largely a result of changes in the Euro/ dollar exchange rate and an increase in certain key executive salaries. Stock compensation expenses were $18,000 in 2002, $23,000 in 2001 and $20,000 in 2000.

Non-operating Items

Other income of $2.5 million in 2002 consisted of the amount received from the Wellcome Foundation in settlement of certain litigation with respect to our product, Genvir. See “Note 9 to Consolidated Financial Statements.”

The French government provides tax credits to companies for annual increased spending for innovative research and development. Income tax benefits correspond to these French research tax credits, which are credited against income taxes payable in each of the four years after being incurred or, if not so utilized, are recoverable in cash. At December 31, 2002, we had total research tax credits receivable of $900,000. If these credits are not applied against future income taxes, they will be received as cash payments in 2003 of $260,000 and in 2007 of $630,000. We earned a research and development credit in 2002 of $567,000 and did not have any such credit in 2001 or in 2000. As a result, we recognized a tax benefit of $567,000 in 2002, which resulted primarily from French research and development credits and paid the statutory minimum income tax expense of $14,000 for 2001 and of $50,000 for 2000 including the statutory minimum income tax expense of $16,000, and a $34,000 adjustment from prior years for the fiscal audit concerning research tax credit.

As of December 31, 2002, we had net accumulated French tax loss carryforwards of $30.4 million, which can be credited against future taxes payable. Of this sum, $9.4 million is attributed to the depreciation of capital assets and may be credited against future taxes payable with no time limits. The remaining

$21.0 million must be credited against future taxes payable within four years after being incurred. See “Note 6 to Consolidated Financial Statements.”

Interest income earned on our cash balance was $297,000 in 2002, $292,000 in 2001 and $373,000 in 2000. The changes in interest earned year-to-year is primarily the result of fluctuating average cash balances invested year-to-year and declining interest rates in 2002. Interest expense was $49,000 in 2002, $52,000 in 2001 and $51,000 in 2000 and is primarily related to the interest applicable to our equipment leases.

Change in Accounting Principle

We have historically recognized non-refundable technology access fees received from our collaboration agreements as revenue when received. In December 1999, the SEC issued Staff Accounting Bulletin (SAB) No. 101, “Revenue Recognition in Financial Statements.” Among other things, SAB No. 101 describes the SEC staff’s position on the recognition of certain non-refundable up-front fees received in connection with research collaborations. We have evaluated the applicability of SAB No. 101 in conjunction with our existing collaborative agreements. As a result, effective January 1, 2000, we changed our method of accounting for the receipt of such fees to recognize revenue over the term of the related development period. We recorded the cumulative effect of a change in accounting principle of $4.6 million in the results for the year ended December 31, 2000. For the years ended December 31, 2001 and December 31, 2000, we have recorded $2.8 million and $1.5 million, respectively, of license and research revenue, which was included in the cumulative effect adjustment recorded on January 1, 2000. There was no effect of this accounting principle in 2002.

Net Profit/Loss

For the year ended December 31, 2002, we reported a net profit of $3.0 million, or $0.18 per share on a diluted basis. The net losses reported for the years ended December 31, 2001 and December 31, 2000 were $2.9 million, or $0.18 per share, and $9.5 million, or $0.62 per share, respectively.

Liquidity and Capital Resources

As of June 30, 2003, we had $11.6 million in cash, compared to $11.9 million in cash at the end of the first half of 2002.

As of September 22, 2003, we had approximately $20.9 million in cash, $9.6 million of which is a result of the exercise of warrants, and we expect to receive the initial $20 million payment pursuant to our licensing agreement with Bristol-Myers within several weeks.

Net cash used in operating activities was $4.9 million for the first six months of 2003 compared to $6.4 million provided by operations for the first six months of 2002. The use of cash from operations in 2003 is primarily due to the net loss for the period and increases in accounts receivable partially offset by increases in deferred revenue from recent licensing agreements and exchange rate differences.

Net cash provided by (used in) operating activities was $8.8 million in 2002, $(2.8) million in 2001 and $(5.6) million in 2000. In 2002, net cash provided by operating activities reflected a net income of $3.0 million, a $5.0 million decrease in accounts receivable due to payments of amounts invoiced in 2001 and a net repayment of $938,000 related to research tax credits offset by a $1.4 million decrease in accrued expenses.

Net cash used for capital investments was $1.4 million in 2002, which was primarily spent at the Pessac facility to provide the capacity needed for the ongoing development of our products. Net cash used for capital investments amounted to $1.2 million in 2001 and $737,000 in 2000.

Since our inception, our operations to date have consumed substantial amounts of cash in the aggregate and are expected to continue to do so, at least for the next two years. We believe that ongoing research and product development programs are adequately funded for the next year. We also believe current financial

resources and cash from various grants, royalty payments and licenses will be sufficient to meet our cash requirements for the next twelve months.

At December 31, 2002, we had loans of $927,000 from Anvar, an agency of the French government that provides financing to French companies for research and development. These loans do not bear interest and are repayable only in the event that the research is successful technically or commercially. See “Note 4 to Consolidated Financial Statements.”

We do not maintain any credit lines with financial institutions.

Our contractual cash obligations at December 31, 2002 are as follows:

	Payments Due Per Period				
	Less than 1 year	1 to 3 years	4 to 5 years	More than 5 years	Total
	(In thousands of U.S. dollars)				
Long-term debt	$ 693	$168	$519	$704	$2,084
Capital lease obligation	249	163	—	—	412
Operating leases	290	470	26	—	786
Total contractual cash obligations	$1,232	$801	$545	$704	$3,282

At December 31, 2002, we had no other commercial commitments.

BUSINESS

General Overview

We are a biopharmaceutical company principally engaged in the development of two unique polymer-based delivery technologies for medical applications. Our Micropump technology is a multiparticulate technology for oral administration of small molecule drugs with applications in controlled-release, tastemasking and bioavailability enhancement. Our Medusa nano-particulate technology is designed to deliver therapeutic proteins, peptides and small molecules. Our expertise in polymer science has also been instrumental in the development of a photochromic eyeglass lens product that was launched by Corning in 1999. Additionally, we have developed new herbicide delivery systems and have patented a biomaterial, ColCys®.

Our Medusa technology permits the long-acting controlled-release of proteins without the denaturation or other adverse effects on such proteins of certain other delivery systems. Our initial application of Medusa is Basulin, a long-acting insulin for the treatment of diabetes. Since 1999, we have worked with Novo Nordisk A/S to optimize the Medusa polymer and the insulin formulation to be delivered using our proprietary technology. As of March 12, 2002, we reacquired all rights to Basulin. On August 27, 2003, we announced that we had entered into a license agreement with Bristol-Myers for Basulin. The licensing agreement, which is subject to antitrust clearance, provides for an initial payment to us of $20 million, additional milestone payments that could reach $145 million and double-digit royalties on the sale of the product. Bristol-Myers also has assumed all costs of future clinical trials, development, registration and marketing of the product. Applications of Medusa to other therapeutic proteins are in an advanced stage of pre-clinical development, two of which are funded by major pharmaceutical partners and the others are being pursued at our cost.

We currently have three major products based on our Micropump technology: Genvir, a controlled-release acyclovir for the treatment of genital herpes; Metformin XL, a controlled-release form of Metformin currently in development for use for the treatment of Type II diabetes; and Asacard, a controlled-release formulation of aspirin for the treatment of cardiovascular disease. We are in active discussions with a number of potential partners for the further development and registration of our controlled-release Metformin. We have established a partnership with Biovail for the development and marketing of Genvir in the United States and Canada. We are in active discussions seeking to obtain a marketing partner for Asacard.

We have had a long-standing collaborative relationship with Corning to develop advanced polymeric photochromic materials for eyeglass lenses. We have enjoyed almost four years of royalties as a result of sales of this product. This is also the first product containing our technology to be commercialized. Pursuant to agreements with Monsanto Company, we have collaborated to develop a new herbicide delivery system to enhance the penetration of glyphosate, the world’s leading post-emergent herbicide marketed by Monsanto under the brand name Roundup®. Monsanto’s agreement with us in respect to this product has been terminated and we are free to work with other partners in the application of this technology to agricultural uses. Although ColCys, a biomaterial for the prevention of post-surgical adhesions, has shown promise, we have slowed its development.

To date, we have entered into licensing or partnership arrangements with six major corporations to commercialize products incorporating our technologies, to fund development work and, in selected cases, co-develop specific products.

The following table summarizes our drug delivery technologies and identifies the related pharmaceutical and biotechnology company partners in respect of such technologies as of September 22, 2003.

Summary Table of Medusa and Micropump Products

Product Candidate	Indication	Status	Partner
Medusa			
Basulin	Diabetes	Phase II	Bristol-Myers
Interleukin-2	Cancer	Pre-clinical	In-house
Erythropoetin (EPO)	Anemia	Pre-clinical	In-house
Interferonα	Hepatitis C, cancer	Pre-clinical	In-house
Human growth hormone	Short stature	Pre-clinical	In-house
Other feasibility study agreements	Multiple	Pre-clinical	Undisclosed
Micropump			
Genvir	Herpes	Phase III	Biovail (U.S. and Canada)
Metformin XL	Diabetes	Phase II	In discussions
ACE Inhibitor	Cardiovascular disease	Confidential	Servier
Project A	Undisclosed	Confidential	Merck
Augmentin SR	Infectious diseases	Confidential	GlaxoSmithKline
Undisclosed drug	NA	Confidential	GlaxoSmithKline
Asacard (aspirin)	Cardiovascular disease	Approved 11 Countries (Europe)	In discussions
Other feasibility study agreements	Multiple	Confidential	Multiple

The Need for Novel Delivery Systems

Our polymer delivery systems are currently focused on the controlled release of therapeutic proteins and the oral administration of pharmaceutical drugs, primarily those that are best absorbed in the small intestine. The pharmaceutical industry utilizes drug delivery technologies as a tool to improve existing products as well as to overcome certain problems encountered in the development of new products. Drug delivery technologies enable pharmaceutical companies to improve the safety and efficacy profiles of innovative new therapeutic compounds, to improve patient compliance and acceptance of existing drugs, to expand therapeutic indications of an existing drug, and to gain competitive advantages for drugs facing patent expirations. It is estimated that pharmaceutical product sales utilizing advanced drug delivery technologies amounted to approximately $38 billion worldwide in 2002.

Although significant work has been done on improved drug delivery, little of this knowledge has been applied to the agrochemical industry. We believe there is an opportunity in this industry for our technologies to be used toward developing improved agrochemical compounds that offer higher levels of efficiency and efficacy.

Business Strategy

We aim to build on our core strength as a science based, market focused innovator of controlled release drug delivery systems. The key elements of our strategy that will enable us to build upon our strengths are as follows:

- maximize the potential of our existing drug delivery systems;
- develop or acquire additional drug delivery technologies:
  - by identifying additional compounds for unmet medical needs;
  - by developing new formulations of proprietary compounds that we receive from additional collaborators; and

• leverage capabilities of pharmaceutical partners for clinical development and commercialization.

We believe that we have a competitive advantage in developing controlled-release formulations of proteins, peptides and small molecules that improve dosing, compliance and efficacy. We remain committed to focusing on our strengths. We will continue to partner our proprietary formulations with pharmaceutical companies with the clinical, regulatory and marketing resources to secure regulatory approval and to commercialize these pharmaceuticals successfully.

Under our partner agreements, our pharmaceutical company partners typically assume responsibility for all clinical, regulatory and marketing costs and make payments to us at the time the agreement is signed and upon the achievement of significant technical, clinical and regulatory milestones. We also typically are entitled to receive ongoing royalty payments on the sales of pharmaceuticals that incorporate our technologies.

Medusa: Delivery System for Therapeutic Proteins and Peptides

Therapeutic agents based on biological proteins and peptides are becoming increasingly important. The worldwide market for currently approved biological drugs is over $20 billion annually; the growth of this market is expected to be significant as new products are commercialized. In developing these products, a principal challenge is finding a suitable delivery system that can transport the protein or peptide to its site of action, release it at the optimal therapeutic rate, and protect it from being unduly degraded without denaturing it (*i.e.*, causing a structural change that results in a loss of the properties that are linked to its precise structure).

The scientific challenges to developing such a controlled-release process for protein-based drugs are significant. For a polymer-based delivery system, these constraints require a polymer that:

• can be metabolized by the human body into harmless substances;

• is compatible with the protein or peptide;

• keeps the structure of the protein intact;

• protects the therapeutic agent during transit and delivery; and

• has the required release properties once delivered.

Responding to these scientific challenges and to what we believe is a significant market opportunity, we have developed Medusa, a delivery system designed to deliver proteins and peptides in a controlled manner without denaturation. Our approach utilizes a novel nano-particulate system, combined with a customized polyaminoacid biopolymer, that meets the above conditions. We have developed a protein-like polyaminoacid composed of only two different amino acids. We tailor this polyaminoacid polymer to form nano-scaled particles spontaneously in water that entrap proteins without the use of solvents or any surfactants. This “self-assembly” process is critical in avoiding the denaturing of the proteins. We have shown in animal studies that our polyaminoacid polymer is neither immunogenic nor reactogenic.

Basulin: Long-acting Basal Insulin Formulation

Our first application of our proprietary Medusa technology is a depot delivery formulation of insulin targeted to meet the long-acting, “basal” insulin requirements of diabetic patients.

Insulin Market

Insulin serves to regulate the glucose level in the blood. In a non-diabetic person, the body produces insulin in large quantities after each meal to reduce the resulting high glucose level. The body also produces a small quantity of insulin every 15 minutes to ensure that a basal level of insulin is maintained throughout

the day. To maintain similar control over their glucose levels, diabetics who need insulin also require two different types: a fast-acting insulin to be taken at meal times, and a long-acting insulin to maintain a constant minimum level of needed insulin, particularly throughout the night when patients do not inject insulin.

The worldwide market for insulin is in excess of $2.5 billion annually. Of this total, long-acting basal insulin is estimated to constitute $1.3 billion in annual sales. In Type I diabetics (those with Insulin Dependent Diabetes Mellitus), basal insulin represents 40% of their required treatment. Type II diabetics (those with Non-Insulin Dependent Diabetes Mellitus) significantly out-number Type I diabetics and often require only basal insulin. Our Basulin is designed to address the long-acting basal insulin requirements of both of these groups.

The Development of Basulin

Using our Medusa delivery system, we have been able to form nano-particles of human insulin with our proprietary polyaminoacid polymer to produce a long-acting, injectable insulin formulation, Basulin.

We have successfully completed a phase I study of Basulin in Manchester, England. The randomized, double-blind, placebo controlled study was designed to investigate the pharmacokinetic (bioavailability) and pharmacodynamic (efficacy) properties of Basulin using the clamp technique. This protocol determined the duration of efficacy of Basulin in comparison with NPH (Novo Nordisk's commercial long-acting insulin) and with a placebo, with favorable results. This study also evaluated the safety of Basulin. Results from the study are expected to be extremely helpful in mapping out the further development of this important drug.

Prior to entering the clinical testing phase of its development, we extensively evaluated Basulin in a series of pharmacokinetic tests on both dogs and pigs. Basulin consistently exhibited its ability to deliver insulin for a longer period of time than the leading long-acting insulin products currently marketed — for up to 18-24 hours, as compared to 8-12 hours for NPH. In these tests, the Basulin formulation also consistently exhibited release profiles significantly flatter than the other long-acting insulin drugs. Theoretically, a profile with minimal peak and trough differences should minimize a diabetic's hypoglycemia and hyperglycemia (low and elevated blood glucose levels) episodes, particularly during the first hours after insulin injections and during the sleeping hours. In diabetics, large variations in blood glucose levels over time can lead to serious, long-term complications including vision impairment, foot ulcerations and kidney failure. Minimizing the peaks and valleys of a diabetic's blood glucose level is thought to prevent such serious long-term complications.

If the results of the studies performed to date are confirmed in future clinical trials, Basulin could provide significant benefits in terms of improved control of glucose levels in both Type I and Type II diabetics. It should reduce the frequency of insulin injections and, over the long term, it could reduce the medical complications associated with sustained elevated glucose levels. We can offer no assurance, however, that Basulin will provide any of the benefits described above.

In December 1999, we signed a development and licensing agreement with Novo Nordisk, a recognized world leader in insulin and diabetes care. Under the terms of the agreement, we worked with Novo Nordisk to complete the development of Basulin. As of March 12, 2002, our agreement with Novo Nordisk was terminated and we do not expect any further revenues from Novo Nordisk for this project. On August 27, 2003, we announced that we had entered into a license agreement with Bristol-Myers for Basulin. The license agreement, which is subject to antitrust clearance, provides for an initial payment to us of $20 million, additional milestone payments that could reach $145 million and double-digit royalties on the sale of the product once specific sales levels are achieved. Bristol-Myers also has assumed all costs of future clinical trials, development, registration and marketing of the product. See " — Strategic Alliances — Bristol-Myers."

Other Products Based on the Medusa Technology

During 2002, we entered into partnerships with a number of major biotechnology and pharmaceutical companies for application of our technology. Confidentiality provisions in each agreement prevent disclosure

of the partner or the product. We intend to seek to enter into additional partnerships for the application of our Medusa technology in 2003.

In a further effort to leverage our knowledge of Basulin and the Medusa technology, we have sought and received French government funding for research activity related to additional applications of our Medusa technology. These are in the feasibility testing phase.

We believe that the Medusa delivery system has the potential to improve formulations of other important biological drugs. During 2002, research efforts were focused on applying Medusa to interferon alpha to develop a long-acting interferon product. We believe that the efficacy of interferon alpha, particularly in the treatment of Hepatitis C and cancer, can be improved if its half-life in the body can be extended. Initial studies in living animals have shown promising results. Pharmacokinetic studies in rats using the Sprague Dawley Rat model show a continued concentration of a Medusa-enhanced interferon alpha 2b for up to 96 hours, as compared to 8-12 hours for the conventional formulation.

We estimate the worldwide market for interferon drugs to have been $3 billion in 2002, and we expect this market to grow in 2003 as researchers identify additional indications that may be treated effectively using interferon drugs, as such proposed treatments gain approval and as new suppliers emerge. In 2002, we estimate that interferon alpha formulations accounted for approximately 45% of the worldwide market for interferons. Based on the feasibility test results and the attractiveness of the commercial market, we plan to continue the pre-clinical development of this product and hope to partner with one or more companies with respect to further work on interferon in the year 2003.

Micropump: Delivery System for the Oral Administration of Drugs

Our other drug delivery platform, Micropump, is an oral multiparticulate technology with applications in sustained release, tastemasking and bioavailability enhancement.

Micropump provides a method of encapsulating microscopic-sized particles or granulates of a pharmaceutical compound with carefully selected polymers designed to achieve a desired pharmacokinetic profile. These microparticles have dimensions that are intended to control the absorption rate of the drug. Each microparticle acts as an independent drug delivery vehicle that slowly releases particles, since they can be “programmed” for each drug and each therapeutic indication by modifying the thickness and composition of the polymer coatings and the excipients encapsulated with the drug.

We believe that Micropump particles, which measure approximately 200 to 500 microns in diameter, can provide benefits in controlled release and in the tastemasking of bad tasting active materials. The latter use is particularly important where the microparticles are dosed in sachet or liquid suspension, or as rapidly dissolving tablets. In addition, we believe that our Micropump technology can facilitate improvements in the bioavailability of certain drugs whose low solubility profile restricts both the rate and extent of absorption. We have demonstrated that the incorporation of certain hydrophilic excipients into the Micropump particles leads to marked improvements in drug stability which may, in turn, lead to enhancement of bioavailability. We are currently pursuing this application for the Micropump technology. Many new and effective drug compounds demonstrate poor stability characteristics, which can hamper the ability of these compounds to be successfully developed and commercialized. We believe that a drug delivery technology which has application in stabilizing such compounds would have significant value.

Micropump technology has several other key attributes, including a high loading ratio of active ingredient to its polymer coating, thus allowing for conventional size tablets or capsules. This is important for some products, such as acyclovir, where large daily doses are required. The large number of microparticles contained in a tablet or capsule also enhances safety by avoiding the problem of dose-dumping (releasing all of the dose at one time/one place). Dose-dumping can give rise to side effects such as ulceration. In addition, changes in pH levels within a patient’s body have been shown not to affect the Micropump particle coating and this coating uses a class of material approved for pharmaceutical use by the FDA, which may accelerate testing and approval.

Products Based on the Micropump Technology

We believe that our Micropump system is most appropriate for delivery of therapeutic compounds for which the small intestine is the optimal site of absorption and where the extension of mean plasma concentration time is important. We are currently developing the following drugs based on the Micropump system:

1. Genvir: Controlled-release Oral Acyclovir

We have applied our Micropump technology to develop a controlled-release formulation of acyclovir for the treatment of genital herpes.

The Market for Anti-herpes Drugs

We estimate the worldwide market for the treatment of herpes infections to have been approximately $1.7 billion in 2002. Of this, approximately $700 million was attributable to the treatment of genital herpes, including $260 million for the treatment of acute infections. Acyclovir, including multiple generic formulations and Glaxo Wellcome's Zovirax®, is currently the leading drug for the treatment of herpes infections. Two relatively expensive, second-generation prodrugs of acyclovir, GlaxoSmithKline's Valtrex (valacyclovir) and Novartis's Famvir (famciclovir), have recently been gaining market share. These second-generation drugs address a principal weakness of acyclovir: its arduous dosing regimens. For the acute genital herpes and zoster indications, acyclovir needs to be taken five times per day; for chronic genital herpes indications, acyclovir needs to be taken twice per day. These second generation drugs have reduced the dosing schedule to three times per day for zoster, two times per day for acute genital herpes and one to two times per day for chronic genital herpes.

Controlled-release Acyclovir for Acute Genital Herpes

Genvir is an oral drug also offering a twice per day dosing regime for the treatment of acute genital herpes. Using Micropump, we have overcome the obstacles presented by the particular absorption characteristics of acyclovir to improve its pharmacokinetic profile and develop an effective, controlled-release formulation of the drug. Genvir, with a dosing schedule equivalent to Valtrex and Famvir, is positioned as a second-generation treatment for acute genital herpes and as an alternative to the acyclovir prodrugs.

As proven in its European phase III study, Genvir taken twice a day provides the same effective treatment for acute genital herpes as Zovirax (brand-name acyclovir) taken five times a day. The double-blind phase III clinical study of Genvir was conducted in France and Germany with 596 patients enrolled, 423 of whom were treated for an acute attack of genital herpes. In this study, Genvir 600mg taken twice a day was demonstrated to be therapeutically equivalent to Zovirax 200mg taken five times a day. The principal endpoint in the study was the percentage of patients with healed herpes lesions on the fifth day. The study concluded that 53.6% of Genvir-treated patients had healed lesions as compared to 45.7% of Zovirax-treated patients. Additionally, the occurrence of new herpes lesions in the Genvir-treated patients was less than in the Zovirax-treated patients. The safety profiles of both drugs were excellent and similar.

In addition to this patient compliance advantage over regular acyclovir, we believe Genvir will likely be priced significantly below the newer prodrugs when it enters the market. Genvir will also have the added advantages of acyclovir's long-standing record of efficacy and safety and entrenched prescribing and purchasing behaviors that favor acyclovir.

On April 9, 2003, we announced that we had licensed rights to Genvir in the United States and Canada to Biovail. Phase III clinical trials are expected to be conducted by Biovail beginning in 2003. We anticipate using the data from these clinical trials for registration of Genvir outside the United States and Canada upon their completion.

2. Asacard 162.5mg: Controlled-release Cardiovascular Aspirin

The first pharmaceutical product utilizing Micropump is Asacard, a controlled-release formulation of aspirin (acetylsalicylic acid, or ASA) specifically designed for the long-term treatment of cardiovascular diseases with thrombotic origin.

We estimate that at least 9.5 billion doses of aspirin are consumed worldwide each year for cardiovascular treatment, making it the most widely used segment of the aspirin market. According to a significant body of published medical literature, a majority of people who have suffered a heart attack or stroke are advised to take aspirin daily, and many are expected to do so for the remainder of their lives. However, the long-term use of aspirin may give rise to gastrointestinal side effects, including stomach bleeding and stomach and intestinal ulcers. It is generally believed that these side effects are the principal obstacle to an even greater use of cost-effective aspirin for this indication.

To avoid the adverse gastrointestinal side effects of aspirin, two approaches have been proposed to date: enteric coated aspirin and low-dose aspirin. We believe that neither approach provides a satisfactory solution. Enteric coated aspirin formulations attempt to reduce gastric side effects by preventing aspirin from touching the stomach wall, but this solves only a part of the problem. The use of low dose aspirin (75mg per day) is becoming increasingly popular, particularly in the United States. However, daily use of even low doses can give rise to gastrointestinal side effects and, more significantly, some published studies suggest that such low doses may not be effective.

Responding to this need, we developed and patented Asacard, a unique controlled-release, microencapsulated aspirin, based on our Micropump technology. Asacard is designed to provide effective and safe therapy for cardiovascular treatment. Its efficacy for this indication comes from the release of aspirin into the circulatory system where it provides cardiovascular benefits similar to conventional aspirin formulations. We believe, however, that what differentiates Asacard from conventional aspirin is that it reduces gastrointestinal side effects. Asacard is the only aspirin formulation that significantly controls the rate of release of aspirin in the systemic circulation system, thus avoiding the major cause of gastrointestinal problems. Additionally, its microparticle coating protects the stomach and intestine linings from direct contact with the aspirin.

Given current U.S. medical practice that favors the lower, 75mg doses of aspirin for cardiovascular disease and the costs of required U.S. clinical testing, we have deferred plans to further develop this product. The U.S. patent for Asacard was issued in 1997. Recently, however, increasing interest has been expressed in licensing this product and we are engaged in discussions in an effort to seek a partner for a controlled-release, micro-encapsulated product.

3. Other Products Based on Micropump Technology

From time to time we have conducted Micropump feasibility studies on other proprietary therapeutic compounds under limited, confidential agreements with the pharmaceutical companies owning the rights to these compounds. We are currently conducting four such confidential studies in partnership with a number of undisclosed pharmaceutical companies. No new products have yet emerged from the research done on these compounds. We will continue to seek additional partnerships to conduct feasibility studies in the future.

Photochromic Materials

Our expertise in polymer science has led to a long-term collaborative relationship with Corning. Under a contract research arrangement that has existed since 1994, we have worked with Corning to produce two generations of material for photochromic lenses. In 1998, we entered into a long-term collaboration and development agreement with Corning that replaced the existing contract research relationship. See “— Strategic Alliances — Corning: Photochromic Materials.”

Photochromic lenses automatically darken in the presence of sunlight and then revert to clear when indoors. These eyeglass lenses, which are based on mineral material, have been available for over 20 years, and Corning has been the dominant worldwide supplier of these lenses since their introduction. However, as eyeglass lenses have been increasingly made with plastic materials, there is a strong and growing demand for

photochromic lenses based on polymer (plastic) materials. We believe that Corning, which is building an existing franchise and business expertise in the eyeglass lens market, is well positioned to compete effectively in the worldwide market for polymer-based photochromic lens material.

During 1999, Corning launched SunSensor™, a new, competitive photochromic eyeglass lens product containing our technology. We began receiving royalties on the sales of this product late in 1999. The amount of future royalties related to this and other potential products resulting from this collaboration is dependent on Corning's marketing success.

Under terms of our current agreement with Corning, we will continue to receive research and development payments for our work performed under the agreement. In the future, we will receive royalties on sales of all products that contain intellectual property developed by the collaboration. See "— Strategic Alliances — Corning: Photochromic Materials."

Agsome™: Delivery System for Agrochemical Active Ingredients

Several years ago, we launched an effort to apply our know-how in the controlled-release of biopharmaceuticals to the delivery of agrochemical products. Agsome, a patented agrochemical active ingredient delivery system, resulted from these efforts.

The Agsome technology encapsulates active agrochemical ingredients into nano-scaled particles in order to improve their delivery and performance. The resulting increase in efficiency of the agrochemical compounds reduces the amount of required active ingredient. This potentially results in lower costs for both producer and user. We believe that the use of less agrochemical active ingredients also could have a positive environmental impact.

To advance our Agsome technology, we collaborated with one of the worldwide leaders in the agrochemical business, Monsanto. Initially, we signed a limited agreement with Monsanto Europe to apply this technology to the leading herbicide, glyphosate, a product commercialized by Monsanto under the brand name Roundup. Late in 1997, we entered into a worldwide agreement with Monsanto that expanded the scope of our collaboration and extended the agreement to all agrochemical active ingredients.

In 1998, the Agsome technology, as applied to glyphosate herbicide, was validated in greenhouse trials by Monsanto. Also in 1998, our collaboration produced seven patent applications related to Agsome technology, particularly as applied to glyphosate herbicide, which are owned by Monsanto. Monsanto is required to pay us royalties if it uses any of this technology in its products.

In August 1999, Monsanto terminated its funding of the joint development efforts for an enhanced formulation of glyphosate herbicide pursuant to this agreement. However, testing of our formulation by Monsanto is continuing.

ColCys Biomaterials

We have developed a novel and proprietary family of biomaterials based upon collagen-cystine called ColCys, which is comprised exclusively of naturally occurring molecules. Collagen materials extracted from various animals are widely used as implantable devices in such fields as plastic and abdominal surgeries.

Collagen is a protein abundantly present in humans and animals and is an excellent building block for designing polymers that are compatible with living animal tissue. However, during extraction and purification processes, collagen typically loses the essential part of its mechanical properties. Our proprietary technology grafts cystine molecules onto individual strands of collagen. The molecules are subsequently crosslinked through simple oxidation/ reduction reactions to form a network between the collagen chains. This network formation mimics that of keratin, a natural building block found in the body's hair and nails. This unique crosslinking technology provides enhanced mechanical properties and a more controllable rate of biodegradation compared with other crosslinking methods that utilize toxic chemical agents such as gluteraldehyde. By controlling the level of crosslinking, the materials' mechanical properties and their speed of biodegradation can be tailored to meet the needs of different applications. ColCys biomaterials can be

prepared in the form of fluids, hydrogels, molded parts, cast films, or coatings, each of which has the ability to be crosslinked either before implantation or in vivo.

ColCys biomaterials' enhanced mechanical properties and more controllable rate of biodegradation appear to make them well suited for medical implant applications.

ColCys for Post-Surgical Adhesion Prevention

We have considered a number of potential applications for ColCys, including use in soft tissue surgical adhesives and, most recently, barriers for the prevention of post-surgical adhesions. With a potential worldwide market that we estimate to be $700 million to $1 billion annually, this application for the prevention of post-surgical adhesions has the largest market potential. Therefore, we have focused our efforts developing a ColCys film that can prevent the formation of adhesions following surgical procedures.

Due to the internal trauma and resulting scarring related to many surgical procedures, unwanted attachments (usually fibrin bands), known as adhesions, form between internal organs and/or surfaces of the body. These adhesions can give rise to excessive and long lasting pain, as well as hinder the organs from functioning properly. Various studies looking at gynecological and abdominal procedures have shown that adhesions occur in 55% to 100% of the cases examined. These two areas of surgery represent over four million procedures each year in the United States alone.

There are a number of different products currently marketed for adhesion prevention, but they have achieved little success primarily because they do not provide a satisfactory, high level of reliability. We believe that for a product to be widely accepted as a preventive for post-surgical adhesion growth it must be consistently effective, *i.e.*, effective more than 80% of the time. Without this high level of assurance, surgeons appear to be reluctant to use it and those paying for medical services may have difficulty justifying the related added cost. By tailoring ColCys' mechanical properties and rate of biodegradation, we believe that we have the potential to produce a film, gel or spray that is better suited for adhesion prevention than other competing products under development.

Further pre-clinical development efforts and external studies are necessary prior to moving into pivotal clinical studies. Faced with cash and resource constraints, we have delayed additional development efforts until partner support or funding is available.

Strategic Alliances

In order to efficiently develop and apply our technologies and effectively commercialize the resulting products, we have entered into, and intend to continue to enter into, collaborative arrangements with large biotechnology and pharmaceutical company partners. Such arrangements typically provide funding for development work and access to target compounds and related know-how and, ultimately, provide distribution capabilities for any resulting products. Such arrangements generally include termination provisions in the event either party decides that, for strategic or other reasons, it does not wish to pursue the alliance. We outline our existing agreements below:

Bristol-Myers

On August 27, 2003, we announced that we had entered into a licensing agreement with Bristol-Myers for Basulin. The license agreement, which is subject to antitrust clearance, provides for an initial payment to us of $20 million, additional milestone payments that could reach $145 million and royalties on the sale of the product. Bristol-Myers also has assumed all costs of future clinical trials, development, registration and marketing of the product.

Biovail

On April 9, 2003, we announced that we entered into an agreement with Biovail to license our Genvir product for the United States and Canada. Except as set forth in such announcement, further terms of the agreement have not been disclosed.

GlaxoSmithKline

On June 18, 2002, we entered into a licensing agreement with GlaxoSmithKline for application of our Micropump technology to a sachet formulation of Augmentin, a widely used antibiotic. We received $1.5 million upon signing of the agreement and total payments of $3.9 million during the year 2002. On March 28, 2003, we announced that we licensed our Micropump technology to GlaxoSmithKline for an undisclosed product.

Servier

On January 11, 2002, we announced that we entered into a licensing agreement with Servier for application of our Micropump technology to an ACE inhibitor that is proprietary to Servier. We received $3 million upon signing of the agreement and total payments of over $10 million during the year 2002. Further terms of the agreement have not been disclosed.

Merck & Co.

Effective September 30, 2001, we entered into a licensing agreement with Merck for an undisclosed class of products. No other terms of the agreement have been disclosed.

Corning: Photochromic Materials

Corning France, on its own behalf and representing Corning Incorporated and Corning Europe Inc., entered into an agreement with us in March 1994 for the co-development of proprietary, polymer-based photochromic eyeglass lens material to be sold by Corning to manufacturers of ophthalmic lenses worldwide. Under this agreement, from March 1994 to February 1998, Corning financed our related research and development costs. This agreement also entitled us to royalty payments based on Corning's net sales, if any, of ophthalmic products that contained materials developed in conjunction with us.

On December 31, 1998, we entered into a new, long-term collaboration and development agreement with Corning S.A. and Corning Incorporated that expanded the scope and applicability of the earlier agreement. Under this new agreement, Corning owns all intellectual property developed with us. However, under specified conditions, we will have the right to use technology developed under the collaboration for applications other than photochromic eyeglass lenses or sunglass lenses. While we previously were entitled to receive royalties on the sales of all products containing intellectual property resulting from the collaboration, the new agreement provides for an increase in royalties on sales of certain products. We received an initial $2.0 million payment and will continue to receive periodic payments from our research and development work under an annually agreed upon work program.

In 1999, Corning launched its first photochromic plastic eyeglass lens product developed in collaboration with us, and we began receiving quarterly royalty payments under this agreement. The year 2002 was the third full year of royalties for us for this product, and we received approximately $900,000 in royalties. We also received periodic payments for our research and development efforts under this agreement. Also in 2002, as in prior years, we sold Corning quantities of photochromic material needed for the production of the new lens product.

Manufacturing

Effective December 31, 1996, we acquired a pharmaceutical production facility of approximately 60,000 square feet located in Pessac, France from SmithKline. See "— Description of Property." As part of the acquisition, we employed 42 experienced plant personnel and entered into a three-year contract manufacturing agreement with SmithKline for cimetidine formulations. We have consistently met SmithKline's production requirements. The agreement was extended through the year 2002, and the parties have agreed to extend this manufacturing arrangement for at least another year.

The Pessac facility provides us with the capability to manufacture our pharmaceutical products. Since acquiring the facility, we have completed certain modifications to the facility, including the addition of a new

manufacturing suite with advanced spray-coating equipment. We believe that the facility and its operations are in substantial compliance with GMP requirements. The facility is also approved by European drug agencies for production of certain pharmaceutical products, including commercial quantities of our microencapsulated drugs. Such approval qualifies us to manufacture certain pharmaceutical products for sale in most countries in Europe. In 1999 we added a new clean room needed for the synthesis of the Basulin biopolymer to the Pessac facility, and it was further enhanced in the year 2000.

During 2002, our chemical production activities were conducted using highly specialized equipment installed at our pilot plant in a leased facility in Vénissieux, France. In 1999, 2000 and 2001, we produced commercial quantities of photochromic material for Corning at this leased facility. We sold our interest in this facility and equipment in January and February of 2003 generating a gain of $376,000. Corning will obtain its requirements for photochromic polymers from other sources as of this date.

In addition to production activities related to our core businesses, we are attempting to build on our capabilities and experience with GlaxoSmithKline and other pharmaceutical customers. With our experienced workforce and current GMP operations, we can provide clinical batch manufacturing, process scale-up services and toll manufacturing of solid dosage forms, as well as provide analytical services for contract customers.

Patents and Proprietary Technology

Patents and other proprietary rights are important to our business. As a matter of policy we seek patent protection of our inventions and trademarks and also to rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. Generally, we first file a patent application covering an invention in France and then file counterpart applications for the invention within one year in other countries.

Since inception, we have been granted 200 patents, including 21 in the United States and 179 worldwide. Among others, these include French patents that relate to microencapsulated aspirin, methods of producing polyaminoacids for use in delivering proteins and peptides, and patents on certain ColCys biomaterials. In the case of the French patents, we currently have counterpart patents or patent applications pending in other European nations, Japan and the United States. We have several additional patent applications pending in France, other European nations, Japan, the United States and some additional countries.

In 2002, we were granted five new patents (two in the United States and three worldwide). Throughout 2002, we filed for 12 new patents (nine in France and three international, including the United States).

We can offer no assurance that any patents issued to us will provide us with competitive advantages or will not be infringed, challenged, invalidated or circumvented by others, or that the patents or proprietary rights of others, will not have an adverse effect on our ability to do business.

There can be no assurance that we will be granted patents in respect of the claims in any of our currently pending or future patent applications, and we can offer no assurance that in the event any claims in any of our issued patents are challenged by one or more third parties, that any court or patent authority ruling on such challenge will determine that such patent claims are valid and enforceable or sufficiently broad in scope to protect our proprietary rights. Also, the nature of the process for obtaining patents and the extent of protection provided by patent laws varies from country to country. We can offer no assurance, therefore, that the issuance to us in one country of a patent covering an invention will be followed by the issuance to us in other countries of patents covering the same invention or that any judicial interpretation of

such patents will be uniform in multiple jurisdictions. Furthermore, even if our patents are determined to be valid, enforceable and broad in scope, we can offer no assurance that competitors will not be able to design around such patents.

Government Regulation

We believe our delivery systems, when used in conjunction with therapeutic pharmaceuticals, will be subject to drug and biological approval requirements. In the United States, biological drugs, such as therapeutic proteins and peptides, generally are subject to the same FDA regulatory requirements as other drugs, although some differences exist. For example, a biologic license application (BLA) is submitted for approval for commercialization instead of the new drug application (NDA) used for other drugs. Also, unlike drug products, biological products are subject to FDA lot-by-lot release requirements and cannot be the subject of abbreviated new drug applications (ANDAs). Insulin, which is regulated as a drug product, typically has not been the subject of ANDAs. However, the FDA is working on a variety of issues pertaining to the possible development of generic versions of insulin and there can be no assurance that this type of submission will continue to be unavailable for insulin. Our delivery systems might also be regulated by the FDA as "combination products" if they are used together with a biologic or medical device. In order to facilitate pre-market review of combination products, the FDA designates one of its centers to have primary jurisdiction for the pre-market review and regulation of both components.

Agrochemical applications of our Agsome formulation can involve a variety of U.S. state and federal environmental laws. The use of this technology in conjunction with herbicides would be subject to registration and other requirements of the U.S. Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). FIFRA requires pesticides (including herbicides) to be registered by the U.S. Environmental Protection Agency (EPA) and authorizes the EPA to prescribe conditions for their use.

Photochromic eyeglass lenses are regulated by the FDA as medical devices, and we believe certain applications of the ColCys biomaterial also would be subject to regulation as a medical device.

The design, testing, manufacturing and marketing of new or substantially modified drugs or medical devices must be cleared or approved by applicable regulations and regulatory agencies, the requirements of which may vary from country to country. This regulatory process is lengthy, expensive and uncertain. In the United States, the FDA regulates such products under various federal statutes, including the Federal Food Drug and Cosmetic Act. Similar requirements exist in the Member States of the European Union. There can be no assurance that we or our collaborative partners will be able to obtain such regulatory clearances or approvals on a timely basis, if at all, for any products under development. Delays in receipt or failure to receive such clearances or approvals, the loss of previously received clearances or approvals, or failure to comply with existing or future regulatory requirements could have a material adverse effect on our business, financial condition and results of operations.

New Drug Development and Approval Process

United States

Regulation by governmental authorities in the United States and other countries is a significant factor in the manufacture and marketing of biological and other drug products and in ongoing research and product development activities. The products of all of our pharmaceutical and biotechnology partners will require regulatory approval by governmental agencies prior to commercialization. In particular, these products are subject to rigorous pre-clinical and clinical testing and other pre-market approval requirements by the FDA and regulatory authorities in other countries. In the United States, various statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of pharmaceutical and biological drug products. The lengthy process of seeking these approvals, and the subsequent compliance with applicable statutes and regulations, require the expenditure of substantial resources.

The FDA's statutes, regulations, or policies may change and additional statutes or government regulations may be enacted which could prevent or delay regulatory approvals of biological or other drug

products. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the U.S. or abroad.

Regulatory approval, when and if obtained, may be limited in scope. In particular, regulatory approvals will restrict the marketing of a product to specific uses. Approved biological and other drugs, as well as their manufacturers, are subject to ongoing review. Discovery of previously unknown problems with these products may result in restrictions on their manufacture, sale or use or in their withdrawal from the market. Failure to comply with regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or injunction, as well as other action affecting our pharmaceutical and biotechnology partners' potential products or uses. Any failure by our pharmaceutical and biotechnology partners to obtain and maintain, or any delay in obtaining, regulatory approvals could materially adversely affect our business.

The process for new drug approval has many steps, including:

Pre-clinical testing

Once a biological or other drug candidate is identified for development, the drug candidate enters the pre-clinical testing stage. Pre-clinical tests include laboratory evaluation of product chemistry and other characteristics and animal studies to assess the potential safety and efficacy of the product as formulated. Pre-clinical tests must be conducted in compliance with good laboratory practice regulations. Violations of these regulations can, in some cases, lead to invalidation of the studies, requiring such studies to be replicated. In some cases, long-term pre-clinical studies are conducted while clinical studies are ongoing.

Investigational new drug application

The entire body of pre-clinical development work necessary to administer investigational drugs to human volunteers or patients is summarized in an investigational new drug (IND) application to the FDA. The IND becomes effective if not rejected by the FDA within 30 days after filing. There is no assurance that the submission of an IND will eventually allow a company to commence clinical trials. All clinical trials must be conducted under the supervision of a qualified investigator in accordance with good clinical practice regulations. These regulations include the requirement that all subjects provide informed consent. In addition, an institutional review board (IRB), comprised primarily of physicians and other qualified experts at the hospital or clinic where the proposed studies will be conducted, must review and approve each human study. The IRB also continues to monitor the study and must be kept aware of the study's progress, particularly as to adverse events and changes in the research. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if adverse events occur.

Clinical Trials

Clinical testing involves the administration of the drug or biologic to healthy human volunteers or to patients under the supervision of a qualified principal investigator, usually a physician, pursuant to an FDA reviewed IND "protocol," or clinical plan. Clinical trials are typically conducted in three sequential phases, but the phases may overlap. Phase I trials consist of testing the product in a small number of patients or normal volunteers, primarily for safety, in one or more dosages, as well as characterization of a drug's pharmacokinetic and/or pharmacodynamic profile. In phase II, in addition to safety, the efficacy of the product is evaluated in a patient population. Phase III trials typically involve additional testing for safety and clinical efficacy and an expanded population at geographically dispersed sites. All patients involved in a clinical trial must provide informed consent prior to their participation. The FDA may order the temporary or permanent discontinuance of a clinical trial at any time for a variety of reasons, particularly if safety concerns arise. Such holds can cause substantial delay and in some cases may require abandonment of a product. These clinical studies must be conducted in conformance with FDA's bioresearch monitoring regulations.

Chemical and formulation development

Concurrent with clinical trials and pre-clinical studies, companies also must develop information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with good manufacturing practice (GMP) requirements. The manufacturing process must be capable of consistently producing quality batches of the product and the manufacturer must develop methods for testing the quality, purity and potency of the final products. Additionally, appropriate packaging must be selected and tested and chemistry stability studies must be conducted to demonstrate that the product does not undergo unacceptable deterioration over its shelf-life.

New drug application or biological license application

After the completion of the clinical trial phases of development, if the sponsor concludes that there is substantial evidence that the drug or biological candidate is effective and that the drug is safe for its intended use, an NDA or BLA may be submitted to the FDA. The application must contain all of the information on the drug or biological candidate gathered to that date, including data from the clinical trials, information pertaining to the preparation of the drug or biologic, analytical methods, product formulation, details on the manufacture of finished products and proposed product packaging and labeling. NDAs and BLAs are often over 100,000 pages in length. Submission of an NDA or BLA does not assure FDA approval for marketing.

The FDA reviews all NDAs and BLAs submitted before it accepts them for filing. It may request additional information rather than accepting an application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA or BLA. As part of this review, the FDA may refer the application to an appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation. The FDA is not bound by the recommendation of an advisory committee. Under the Prescription Drug User Fee Act (PDUFA), submission of an NDA with clinical data requires payment of a fee. In return, the FDA assigns a goal of 10 months from acceptance of the application to return of a first “complete response,” in which the FDA may approve the product or request additional information. There can be no assurance that an application will be approved within the performance goal timeframe established under PDUFA. On the other hand, if the FDA’s evaluation of the NDA or BLA is not favorable, the FDA may refuse to approve the application or issue a non-approvable letter.

Among the conditions for NDA or BLA approval is the requirement that each prospective manufacturer’s quality control and manufacturing procedures conform to GMP standards and requirements. Manufacturing establishments often are subject to inspections prior to NDA or BLA approval to assure compliance with GMPs and with manufacturing commitments made in the relevant marketing application.

Other Countries

Whether or not FDA approval has been obtained, approval of a pharmaceutical product by comparable regulatory authorities must be obtained in any other country prior to the commencement of marketing of the product in that country. The approval procedure may vary from country to country, can involve additional testing, and the time required may differ from that required for FDA approval. Under European Union regulations, product approval can be obtained for a period of five years, renewable subject to certain procedures through either a centralized or decentralized procedure depending on the nature and type of drug. Certain designated drugs are required to use the centralized procedure. All others have the option to use the decentralized procedure, where approval is first obtained in one European Union country that then acts as a reporter for extending the product’s approval in other European Union countries. To the extent possible, clinical trials of our products are designed to develop a regulatory package sufficient for multi-country European Union approval.

Regulatory approval of prices for certain drugs is required in France and in most other countries outside the United States. In particular, certain European countries will condition the reimbursement of a product by the countries’ medical regulatory authorities on the agreement of the seller not to sell the product for more

than a certain price in that country or by unilateral decision of the medical regulatory authorities and to the inscription of a product on a list of reimbursable products. Related pricing discussions and ultimate governmental approvals can take several months to years. Some countries require periodic pricing updates and renewals at intervals ranging from two to five years. We cannot assure you that, if regulatory authorities establish lower prices for any product incorporating our technology in any one European country, this will not have the practical effect of requiring our collaborative partner correspondingly to reduce its prices in other European countries. We can offer no assurance that the resulting prices would be sufficient to generate an acceptable return on our investment in our products.

Regulation of Combination Drugs

Medical products containing a combination of drugs, biological products or medical devices may be regulated as "combination products" in the United States. A combination product generally is defined as a product comprised of components from two or more regulatory categories (*e.g.*, drug/device, device/biologic, drug/biologic). Each component of a combination product is subject to the requirements established by FDA for that type of component, whether a drug, biologic or device.

In order to facilitate pre-market review of combination products, the FDA designates one of its centers to have primary jurisdiction for the pre-market review and regulation of both components. The determination whether a product is a combination product or two separate products is made by the FDA on a case-by-case basis. It is possible that our delivery technologies, when coupled with a drug, biologic or medical device component, could be considered and regulated by the FDA as a combination product.

Marketing Approval and Reporting Requirements

If the FDA approves an NDA or BLA, the product becomes available for physicians to prescribe. The FDA may require post-marketing studies, also known as phase IV studies, as a condition of approval to develop additional information regarding the safety of a product. In addition, the FDA may require distribution to patients of a medication guide for prescription products that the agency determines pose a serious and significant health concern in order to provide information necessary to patients' safe and effective use of such products.

Post-marketing Obligations

Any products manufactured and/or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including record-keeping requirements, reporting of adverse experiences with the product, submitting other periodic reports, drug sampling and distribution requirements, notifying the FDA and gaining its approval of certain manufacturing or labeling changes, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. Drug and biologics manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies. The FDA periodically inspects manufacturing facilities in the United States and abroad in order to assure compliance with the applicable GMP regulations and other requirements. Facilities also are subject to inspections by other federal, foreign, state or local agencies. In complying with the GMP regulations, manufacturers must continue to expend time, money and effort in record keeping and quality control to assure that the product meets applicable specifications and other post-marketing requirements. Failure of the company or our licensees to comply with FDA's GMP regulations or other requirements could have a significant adverse effect on the company's business, financial condition and results of operations.

Also, newly discovered or developed safety or efficacy data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, or even in some instances revocation or withdrawal of the approval.

Patent Restoration and Exclusivity

Under the Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act, a portion of a product's patent term that is lost during a product's clinical development and application review by the FDA may be restored. Hatch-Waxman also provides for a statutory protection,

known as exclusivity, against the FDA's approval or acceptance of certain competitor applications. Patent term restoration can return up to five years of patent term for a patent that covers a new product or its use. The application for patent term extension is subject to approval by the U.S. Patent and Trademark Office (USPTO), in conjunction with the FDA. It takes at least six months to obtain approval of the application for patent term extension, and there can be no guarantee that the application will be granted.

Hatch-Waxman also provides for a period of statutory protection for new drugs approved under an NDA by the FDA. After approval of a "new molecular entity," the FDA may not approve another drug that relies, at least in part, on data from the innovator drug regarding the safety and efficacy of the same active ingredient for five years. Similarly, following approval of an NDA for a previously approved active ingredient (usually a supplemental NDA for a new indication or formulation), the FDA is prohibited from approving another drug that relies, at least in part, on data from the innovator drug regarding the safety and efficacy of that new indication or formulation for that same active ingredient for three years. This exclusivity, however, will not bar the approval of completely new NDAs for the same active ingredient if an applicant conducts and submits its own clinical trials and other data necessary for approval.

While Hatch-Waxman provides certain patent restoration and exclusivity protections to innovator drug manufacturers, it also permits the FDA to approve ANDAs for generic versions of such drugs. The ANDA process permits competitor companies to obtain marketing approval for a drug with the same active ingredient for the same uses but does not require the conduct and submission of clinical studies demonstrating safety and efficacy for that product. Instead of safety and efficacy data, an ANDA applicant needs only to submit data demonstrating that its product is bioequivalent to the innovator product.

Finally, Hatch-Waxman requires an applicant for a drug that relies, at least in part, on data from the innovator drug regarding the safety and efficacy of the same active ingredient, to notify us and/or our business partners of their application and potential infringement of our patent rights. Upon receipt of this notice, we and/or our business partners would have 45 days to bring a patent infringement suit in federal district court against the company seeking to use our data or otherwise violate our patent rights. The discovery, trial and appeals process in such suits can take several years. If such a suit is commenced, Hatch-Waxman provides a 30-month stay on the approval of the competitor's application. If the litigation is resolved in favor of the generic applicant or the challenged patent expires during the 30-month period, the stay is lifted and the FDA's review of the application may proceed.

Regulation of Medical Devices

Some applications for ColCys biomaterial (such as use to prevent post-surgical adhesions) would most likely be classified by regulatory authorities as a medical device.

United States

In the United States, medical devices are classified into Class I, II or III on the basis of the controls deemed by the FDA to be reasonably necessary to ensure their safety and effectiveness. Class I devices are subject to general controls (e.g., labeling, and adherence to cGMPs) and Class II devices are subject to special controls (e.g., performance standards, postmarket surveillance, patient registries, and FDA guidelines). Generally, Class III devices are those which must require premarket approval by the FDA to ensure their safety and effectiveness (e.g., life-sustaining, life-supporting and implantable devices or those found not to be substantially equivalent to legally marketed devices). We believe our ColCys biomaterial for some users will be Class III devices that require premarket approval based on clinical trials. These approvals require proof of the safety and effectiveness of the device to the FDA's satisfaction based upon extensive pre-clinical and clinical trial data. Even after the FDA permits a device to enter commercial distribution (whether Class I, II or III), many potentially costly and time-consuming post-market regulatory requirements apply, such as compliance with the Quality System Regulation (which imposes cGMP requirements) and adverse event reporting.

Other Countries

For medical devices, since January 1, 1995, European Union countries are required to put in effect certain Medical Devices Directives (MDD). This legislation includes, among others, requirements with respect to the design, safety, performance and manufacture of products. Under the system established by the MDD, medical devices must qualify for CE Marking by June 14, 1998. All new medical devices put on the market after June 14, 1998 must meet the MDD requirements. Devices are subject to, in addition to existing or future European Union or other countries' legislation, continued national regulation on pricing and reimbursement that may vary from country to country.

In order to qualify for CE Marking, the manufacturer must comply with the safety and performance requirements of the MDD. In order to demonstrate compliance, the manufacturer must undergo conformity assessment that depends on the class of the product. Once all the necessary conformity assessment tasks have been completed, CE Marking may be affixed on the products concerned. Although member countries must accept for marketing medical devices bearing a CE Marking without imposing further requirements related to product safety and performance, national regulatory authorities who are required to enforce compliance with requirements of the MDD can restrict, prohibit and recall CE Marked products if they are unsafe. Member countries can impose additional requirements as long as they do not violate the MDD or constitute technical barriers to trade. Within the European Union, premarket compliance for certain devices must be supported by clinical data of a type and to the extent set out by the European Union directives and applicable member country regulations. Following marketing, a strict vigilance system involving the reporting of incidents and the appropriate measures to deal with these incidents exists in certain European Union countries, including France.

Other Regulation

GMP rules apply to the manufacturing of drugs and medical devices. Our manufacturing facilities and laboratories are subject to inspection and regulation by French regulatory authorities and may also be subject to the United States and other countries' regulatory agencies. Mutual recognition agreements for government inspections exist between the United States, the European Union, Canada, Australia and New Zealand.

In addition to regulations enforced by the FDA, we are also subject to French, U.S. and other countries' rules and regulations governing permissible laboratory activities, waste disposal, handling of toxic, dangerous or radioactive materials and other matters. Our research and development involves the controlled use of hazardous materials, chemicals, viruses and various radioactive compounds. Although we believe that our safety procedures for handling and disposing of such materials comply with the standards prescribed by French, U.S. and other foreign rules and regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated.

Healthcare Reimbursement

In both U.S. and foreign markets, sales of our potential products, if any, will depend in part on the availability of reimbursement by third-party payers, such as government health administration authorities, private health insurers and other organizations. The U.S. market for pharmaceutical products is increasingly being shaped by managed care organizations, pharmacy benefit managers, cooperative buying organizations and large drugstore chains. Third-party payers are challenging the price and cost effectiveness of medical products and services. Uncertainty particularly exists as to the reimbursement status of newly approved healthcare products. There can be no assurance reimbursement will be available to enable us to maintain price levels sufficient to realize an appropriate return on our product development investment. Legislation and regulations affecting the pricing of pharmaceuticals may change before our proposed products are approved for marketing and any such changes could further limit reimbursement for medical products and services.

Competition

We compete with academic laboratories, research institutions, universities, joint ventures, and other pharmaceutical and biotechnology companies, including other companies developing drug delivery systems. Some of these competitors are also our business partners.

There are other companies developing sustained release drug delivery systems and oral delivery systems. There could be new chemical entities that are being developed that, if successful, could compete against our technologies or products. Among the many experimental therapies being tested in the United States and in Europe, there may be some that we do not now know of that may compete with our drug delivery systems or products in the future. These chemical entities and new products may turn out to be safer or may work better than our technologies or products. Our collaborators could choose a competing drug delivery system to use with their drugs instead of one of our drug delivery systems.

Many of our competitors have substantially greater experience and research and development, manufacturing, marketing, financial and managerial resources than we do. Moreover, there can be no assurance that our competitors will not obtain patent protection or other intellectual property rights that would make it difficult or impossible for us to compete with their products. Furthermore, acquisitions of competing drug delivery companies by large pharmaceutical companies could enhance our competitors' resources. Accordingly, our competitors may succeed in developing competing technologies and products, obtaining regulatory approval and gaining market share for these products more rapidly than we do.

Further, major technological changes can happen quickly in the biotechnology and pharmaceutical industries. Such rapid technological change, or the development by our competitors of technologically improved or different products, could render our drug delivery systems obsolete or noncompetitive.

Additionally, the competitive nature of our industry could adversely affect market acceptance of our products or the use of our drug delivery technologies. Our products and technologies may not gain market acceptance among physicians, patients, healthcare payers and the medical community. The degree of market acceptance of any product candidate that we develop will depend on a number of factors, including:

- demonstration of its clinical efficacy and safety;
- its cost-effectiveness;
- its potential advantage over alternative treatment methods; and
- the marketing and distribution support it receives.

Description of Property

Our corporate headquarters and the research center are located in Vénissieux, France (a suburb of Lyon) in three adjacent leased facilities totaling approximately 26,000 square feet. One building of approximately 13,000 square feet houses the corporate offices and research laboratories, including a clean room equipped for organic synthesis and polymerization, polymer formulation, small scale processing, materials analysis and quality control. The lease on this facility currently expires in 2009, and we intend to renew it. The other 10,000 square foot facility houses a biological laboratory, certain development functions, and our administrative functions. Our leases on this facility expire from 2005 to 2010. The third facility of approximately 3,000 square feet houses our administrative offices. The leases on this facility expire from 2010 to 2013.

We also maintained a 23,000 square foot leased facility at another site in Vénissieux that houses our chemical manufacturing operations. Until 2002, these chemical facilities were used for the manufacturing of the photochromic material that we supplied to Corning. In January 2003, we sold our interest in the facility and our equipment.

In 1996 we acquired a pharmaceutical production facility of approximately 60,000 square feet located in Pessac, France from SmithKline. The plant is housed on a 470,000 square foot lot in an industrial park not far from the Bordeaux airport. Since acquiring the plant, we have added a new manufacturing site with spray-coating equipment and a clean room for the synthesis of biopolymers. The facility has been audited by European drug agencies and is cGMP compliant. It is qualified to manufacture pharmaceutical products that can be sold in most countries in Europe. The value of the facility is recorded in our financial books at the value of the liabilities corresponding to the retirement indemnities of the plant staff that we assumed at the time of the plant purchase, plus the additional investments made by us, less the depreciation and appropriate amortization.

In 2002, activities at this facility included contract manufacturing for GlaxoSmithKline and other major pharmaceutical companies, process and scale-up activities and the production of clinical batches for our own products, and support analytical services for SmithKline and other pharmaceutical laboratories. As our products are commercialized, we expect that this facility will provide necessary quantities of some portion of our products.

Employees

As of September 30, 2003, we had 162 full-time employees. The following table sets forth the number of employees for each of the last three years based in their principal geographic locations.

Year End	Vénissieux(1)	Pessac(2)	U.S.(3)	Total
2000	78	56	3	137
2001	79	57	2	138
2002	80	67	3	150

(1) Primarily engaged in research activities

(2) Primarily engaged in technical and pharmaceutical development activities

(3) Primarily engaged in administrative and marketing activities

We believe that our employee relations are good. As required by French law, we have created an Employee Representation Committee (*Comité d'Entreprise*) comprised of representatives elected from among the personnel. Two of these representatives are entitled to attend all meetings of our board of directors and our shareholders, but they do not have any voting rights.

As of February 1, 2000, French employers became subject to a new law reducing the workweek to 35 hours. In this respect, we signed an agreement relating to our employees located in Vénissieux with representatives of our employees on July 28, 2000 and an agreement relating to our employees located in Pessac in January 2000.

In addition, employment contracts with all of our employees in France are subject to the provisions of either the *convention collective* Chemistry or the provisions of the *convention collective* Pharmacy, the two collective bargaining agreements applicable to employees in our industry.

Litigation

Wellcome Foundation Limited, an affiliate of Glaxo Wellcome, initiated a civil action against us in the *Tribunal de Grande Instance de Paris* on September 17, 1997, claiming infringement of its proprietary rights over the acyclovir molecule. Wellcome Foundation sought damages in an unspecified amount and provisional damages of FF 3 million. We disputed the infringement claim and counterclaimed, alleging that Wellcome Foundation acted in bad faith and used unfair methods of competition. The *Tribunal de Grande Instance de Paris* heard the case on November 6, 2000, and rendered a judgment in our favor on February 20, 2001 and ordered Wellcome Foundation to pay us FF 6 million in damages. In January 2002, we entered into a

settlement agreement with Wellcome Foundation with respect to this litigation, and we received an additional payment of approximately $1.5 million in connection therewith.

While we may be engaged in various claims and legal proceedings in the ordinary course of business, we are not involved (whether as a defendant or otherwise) in and, other than as described above, we have no knowledge of any threat of, any litigation, arbitration or administrative or other proceeding which management believes will have a material adverse effect on our consolidated financial position or results of operations.

MANAGEMENT

Gérard Soula is our founder and has been *Président-Directeur Général* (President and Chief Executive Officer) and Director of Research and Development and a member of our Board of Directors since 1990. Dr. Soula earned a degree from the *Institut d'Administration des Entreprises* in 1971. After receiving his *Doctorat-ès Sciences* in organic chemistry from Marseille University in 1973, he joined Rhône-Poulenc's Research Center in Lyon, France. In 1984, he received the Rhône-Poulenc Innovation Award for his discovery of TDA, a phase transfer catalyst. From 1981 to 1990, he was the Head of Research of the Silicon Group and then Director of Research of the Polymer Materials Department of Rhône-Poulenc.

Stephen H. Willard is our Executive Vice President, Chief Financial Officer and General Counsel and also serves on our Board of Directors. Immediately prior to joining us in August, 2000, Mr. Willard was employed as a vice president of Biovail. He also worked as an investment banker at Credit Suisse First Boston and as an attorney with Gibson, Dunn & Crutcher LLP and Shearman & Sterling LLP. He is a graduate of Yale Law School (1985) and Williams College (1982).

Rafael Jorda is our Vice President, Director of Manufacturing and Development. Mr. Jorda joined us in 1991 and specializes in chemical engineering and in the structure-property relationships of materials. From 1986 to 1990, he worked as a research and development scientist on controlled-released and biopolymers at Rhône-Poulenc.

Rémi Meyrueix is our Scientific Director. Mr. Meyrueix holds the degree of engineer in physics and a doctoral thesis in physics, which he received from the Polytechnic Institute of Grenoble in 1977 and 1980, respectively. He worked at Rhône Poulenc from 1982 to 1990 and joined us in early 1991 as a research engineer. He is now managing the Galenic and Applications platforms in Vénissieux, France.

Roger Kravtzoff is our Pharmaceutical Development Director. Mr. Kravtzoff received his *Doctorat-ès Sciences* in Biochemistry from Tours University in 1988. In 1985, he joined *Centre Régional de Transfusion Sanguine* as a research engineer, and in 1991, he became a scientist associate director in one of its subsidiaries, Novacell. He joined Biovector Therapeutics in 1993 and worked as a Project Director. He joined us in June 2002 and is currently managing our regulatory affairs with regard to our pre-clinical and clinical developments.

Valérie Danaguezian is our Controller for Research and Development Activities. Ms. Danaguezian graduated from the business school of the *Institut Supérieur du Commerce de Paris*. She spent four years working as a statutory auditor with a company that is a member of the Deloitte & Touche group. In 1991, she joined Aventis Pasteur in Lyon where she was in charge of the financial consolidation of the group and was then promoted to Director of Research and Development — Controlling Department. She joined us in May 2003.

You Ping Cheong Chan is our Chemistry Department Director. Mr. Chan received his *Doctorat-ès Sciences* in Chemistry from Strasbourg University in 1990. He joined us in 1992 as a scientist research engineer after spending one year post-doctorate at the Massachusetts Institute of Technology.

SELLING SHAREHOLDERS

The following table sets forth information with respect to the selling shareholders and the ADSs beneficially owned by each selling shareholder that will be offered under this prospectus supplement.

Name of Beneficial Owner	Number of Ordinary Shares or ADSs Owned Prior to the Offering(1)	Number of ADSs Offered(2)	Number of ADSs in Overallotment	Number of Ordinary Shares or ADSs Owned After Completion of the Offering(2)
Alta BioPharma Partners, LP [3]	1,351,954	1,181,017	170,937	170,937
Flamel Chase Partners (AltaBio), LLC[3]	772,088	674,468	97,620	97,620
Alta Embarcadero BioPharma Partners, LLC[3]	50,958	44,515	6,443	6,443
J.P. Morgan Partners (BHCA), L.P.	101,500	88,500	13,000	13,000
Gerard Soula	689,245	—	300,000	689,245

(1) Includes options currently exercisable and exercisable within 60 days.

(2) Assumes no exercise of the overallotment option.

(3) Alta Partners directly or indirectly provides investment advisory services to various venture capital funds, including Alta BioPharma Partners, L.P. (Alta BioPharma), Alta Embarcadero BioPharma Partners, LLC (Alta Embarcadero) and Flamel Chase Partners (AltaBio), LLC. The general partner of Alta BioPharma, members of Alta Embarcadero and the managing member of Flamel Chase exercise sole voting and investment power with respect to the shares held by the funds.

Certain principals of Alta Partners are managing directors of Alta BioPharma Management Partners, LLC, Alta/Chase Management Partners LLC (the General Partner of Alta BioPharma and the Managing Member of Flamel Chase), and members of Alta Embarcadero. As managing directors and members, they may be deemed to share voting and investment powers of the shares held by the funds. These principals disclaim beneficial ownership of all such shares held by the aforementioned funds, except to the extent of their proportionate pecuniary interests therein.

UNDERWRITING

On July 31, 2003, our shareholders authorized the board of directors of Flamel to increase our share capital in connection with this offering through the issuance of up to a maximum of 2,000,000 new ordinary shares. The shares are to be issued in favor of one underwriter, to be selected by our board of directors among the nine underwriters approved by the shareholders. On September 16, 2003, our board of directors selected Merrill Lynch, Pierce, Fenner & Smith Incorporated as the underwriter and sole subscriber for the 2,000,000 new ordinary shares. The participation in this offering by an executive officer of Flamel, the issuance of the new shares and the price at which the shares are to be issued and sold will be determined by our board of directors at a duly authorized meeting.

Subject to the terms and conditions of a subscription and purchase agreement to be entered into among us, the selling shareholders and the underwriters, we will issue 2,000,000 new ordinary shares for subscription by Merrill Lynch, Pierce, Fenner & Smith Incorporated, and Merrill Lynch, Pierce, Fenner & Smith Incorporated will subscribe for such shares, all in accordance with French law. Merrill Lynch, Pierce, Fenner & Smith Incorporated will offer and sell these shares to the public and/or to and/or through UBS Securities LLC, SG Cowen Securities Corporation, Punk, Ziegel & Company, L.P., Merriman Curhan Ford & Co., Brean Murray & Co., Inc. and Puglisi & Co., Inc. in the form of ADSs. Additionally, subject to the terms and conditions of the subscription and purchase agreement, the selling shareholders will agree to sell and the several underwriters will agree to purchase 1,988,500 ordinary shares, in the form of ADSs. The shares will be offered through the several underwriters as listed opposite their names below.

Underwriter	Number of Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated	2,138,675
UBS Securities LLC	777,700
SG Cowen Securities Corporation	388,850
Punk, Ziegel & Company, L.P.	194,425
Merriman Curhan Ford & Co.	194,425
Brean Murray & Co., Inc.	194,425
Puglisi & Co., Inc.	100,000
Total	3,988,500

The underwriters have agreed to subscribe for and purchase all of the shares sold under the subscription and purchase agreement if any of these shares are subscribed for and purchased. If an underwriter defaults, the subscription and purchase agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the subscription and purchase agreement may be terminated.

We and the selling shareholders have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued or sold to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the subscription and purchase agreement, such as the receipt by the underwriters of officer's certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us and the selling shareholders that the underwriters propose initially to offer the shares to the public at the initial public offering price on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of $1.20 per share. The underwriters may allow, and the dealers may reallow, a discount not in excess of $.10 per share to other dealers. After the initial public offering, the public offering price, concession and discount may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us and the selling shareholders. The information assumes either no exercise or full exercise by the underwriters of their overallotment option.

	Per ADS	Without Option	With Option
Public offering price	$33.25	$132,617,625	$152,168,625
Underwriting discount	$1.995	$7,957,058	$9,130,118
Proceeds, before expenses, to Flamel Technologies	$31.255	$62,510,000	$62,510,000
Proceeds, before expenses, to the selling shareholders	$31.255	$62,150,568	$80,528,508

The expenses of the offering, not including the underwriting discount, are estimated at $375,000 and are payable by us and the selling shareholders.

Overallotment Option

The selling shareholders have granted an option to the underwriters to purchase up to 588,000 additional shares at the public offering price less the underwriting discount. The underwriters may exercise this option for 30 days from the date of this prospectus supplement solely to cover any overallotments. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the subscription and purchase agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We and the selling shareholders and our executive officers and directors have agreed not to sell or transfer any ordinary shares for 90 days after the date of this prospectus supplement without first obtaining the written consent of Merrill Lynch. This agreement is subject to certain limited exceptions, including the fact that Stephen Willard, one of our executive officers and directors, may sell up to 100,000 ordinary shares during the 90-day period. Specifically, we and these other individuals have agreed not to directly or indirectly

- offer, pledge, sell or contract to sell any ordinary shares,
- sell any option or contract to purchase any ordinary shares,
- purchase any option or contract to sell any ordinary shares,
- grant any option, right or warrant for the sale of any ordinary shares,
- lend or otherwise dispose of or transfer any ordinary shares,
- request or demand that we file a registration statement related to the ordinary shares, or
- enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any ordinary shares whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lockup provision applies to ordinary shares and to securities convertible into or exchangeable or exercisable for or repayable with ordinary shares. It also applies to ordinary shares owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

Quotation on the Nasdaq National Market

Our ADSs are quoted on the Nasdaq National Market under the symbol "FLML."

NASD Regulations

Because more than ten percent of the net proceeds of the offering may be paid to members or affiliates of members of the National Association of Securities Dealers, Inc. participating in the offering, the offering will be conducted in accordance with NASD Conduct Rule 2710(c)(8). Pursuant to that rule, the appointment

of a qualified independent underwriter is not necessary in connection with this offering, as a bona fide independent market (as defined in the NASD Conduct Rules) exists for our ordinary shares.

Price Stabilization, Short Positions

Until the distribution of the shares is completed, SEC rules may limit underwriters from bidding for and purchasing our ordinary shares. If the underwriters create a short position in the ordinary shares in connection with the offering, *i.e.*, if they sell more shares than are listed on the cover of this prospectus supplement, the representatives may reduce that short position by purchasing shares in the open market. The representatives may also elect to reduce any short position by exercising all or part of the over-allotment option described above. Purchases of the ordinary shares to stabilize its price or to reduce a short position may cause the price of the ordinary shares to be higher than it might be in the absence of such purchases.

Neither we nor any of the underwriters makes any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the ordinary shares. In addition, neither we nor any of the underwriters makes any representation that the representatives or the lead managers will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Passive Market Making

In connection with this offering, underwriters may engage in passive market making transactions in the ordinary shares on the Nasdaq National Market in accordance with Rule 103 of Regulation M under the Securities Exchange Act of 1934 during a period before the commencement of offers or sales of ordinary shares and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

LEGAL MATTERS

Cariddi, Mee, Rué / Hogan & Hartson L.L.P., Paris, France, will provide us with an opinion as to French legal matters and Hogan & Hartson, L.L.P., Baltimore, Maryland will provide us with an opinion as to United States legal matters in connection with the securities we are offering. Certain legal matters in connection with this offering will be passed on for the underwriters by Shearman & Sterling LLP, New York, New York.

EXPERTS

Ernst & Young Audit, independent auditors, have audited our consolidated financial statements at December 31, 2002 and 2001, and for each of the three years in the period ended December 31, 2002, as set forth in their report. We have included our financial statements in the prospectus supplement and the accompanying prospectus in reliance on Ernst & Young Audit's report, given on their authority as experts in accounting and auditing.

FLAMEL TECHNOLOGIES

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

INDEPENDENT AUDITORS' REPORT

The Directors and Shareholders

Flamel Technologies, S.A.

We have audited the accompanying consolidated balance sheets of Flamel Technologies, S.A. ("the Company") as of December 31, 2001 and 2002 and the related consolidated statements of operations, changes in shareholders' equity and cash flows for each of the three years in the period ended December 31, 2002. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company at December 31, 2001 and 2002 and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2002 in conformity with accounting principles generally accepted in the United States.

ERNST & YOUNG AUDIT

Represented by

Jean-Luc Desplat

April 23, 2003
Villeurbanne, France

FLAMEL TECHNOLOGIES S.A.

CONSOLIDATED BALANCE SHEETS

	December 31,	
	2001	2002
	(Amounts in thousands of dollars except share data)	
ASSETS		
Current assets:		
Cash and cash equivalents	$ 5,309	$ 14,527
Accounts receivable	7,596	3,462
Inventory	569	375
Prepaid expenses and other	325	347
Total current assets	13,799	18,711
Property and equipment, net	2,672	3,405
Other assets:		
Research and development tax credit receivable	1,623	890
Other long-term assets	50	70
Total other assets	1,673	960
Total assets	$ 18,144	$ 23,076
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Current portion of long-term debt	$ 391	$ 693
Current portion of capital lease obligations	390	229
Accounts payable	1,205	1,322
Current portion of deferred revenue	1,072	1,805
Advances from customers	1,191	361
Accrued expenses	1,430	2,028
Other current liabilities	782	71
Total current liabilities	6,461	6,509
Long-term debt, less current portion	779	1,391
Capital lease obligations, less current portion	136	149
Deferred revenue, less current portion	2,875	1,952
Other long-term liabilities	384	789
Total long-term liabilities	4,174	4,281
Commitments and contingencies		
Shareholders' equity:		
Ordinary shares: 16,197,590 issued and outstanding at December 31, 2001 and 2002	2,366	2,366
Additional paid-in capital	71,177	71,178
Accumulated deficit	(59,386)	(56,381)
Deferred compensation	(32)	(14)
Cumulative other comprehensive loss	(6,616)	(4,863)
Total shareholders' equity	7,509	12,286
Total liabilities and shareholders' equity	$ 18,144	$ 23,076

See notes to consolidated financial statements.

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year ended December 31,		
	2000	2001	2002
	(Amounts in thousands of dollars except share data)		
Revenue:			
License and research revenue	$ 6,619	$ 9,858	$ 14,593
Product sales and services	3,034	2,009	2,865
Other revenues	1,249	1,220	948
Total revenue	10,902	13,087	18,406
Costs and expenses:			
Cost of goods and services sold	(2,863)	(2,166)	(2,373)
Research and development	(9,789)	(10,662)	(12,239)
Selling, general and administrative	(3,435)	(3,391)	(3,999)
Stock compensation expense	(20)	(23)	(18)
Total	(16,107)	(16,242)	(18,629)
Loss from operations	(5,205)	(3,155)	(223)
Interest expense	(51)	(52)	(49)
Interest income	373	292	297
Foreign exchange gain (loss)	49	55	(99)
Other income	—	—	2,526
Income (loss) before income taxes and the cumulative effect of a change in accounting principle	(4,834)	(2,860)	2,452
Income tax profit (expense)	(50)	(14)	553
Net income (loss) from operations before cumulative effect of a change in accounting principle	(4,884)	(2,874)	3,005
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition (Note 1.4)	(4,577)	—	—
Net income (loss)	$ (9,461)	$ (2,874)	$ 3,005
Earnings (loss) per share before cumulative effect of a change in accounting principle	$ (0.32)	$ (0.18)	$ 0.19
Cumulative effect per share on prior years (to December 31, 1999) of changing method of revenue recognition	$ (0.30)	$ —	$ —
Basic earnings (loss) per ordinary share	$ (0.62)	$ (0.18)	$ 0.19
Diluted earnings per share	$ (0.62)	$ (0.18)	$ 0.18
Pro-forma amounts assuming the change in accounting principle had been applied retroactively:			
Net income (loss)	$ (4,884)	$ (2,874)	$ 3,005
Basic earnings (loss) per ordinary share	$ (0.32)	$ (0.18)	$ 0.19
Diluted earnings per share	$ (0.32)	$ (0.18)	$ 0.18
Weighted average number of shares outstanding (in thousands):			
Basic	15,331	16,198	16,198
Diluted	15,331	16,198	16,711

See notes to consolidated financial statements.

FLAMEL TECHNOLOGIES S.A.

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY

	Ordinary Shares		Additional Paid-in Capital	Accumulated Deficit	Deferred Compensation	Cumulative Other Comprehensive Loss	Shareholders' Equity
	Shares	Amount					
	(Amounts in thousands of dollars except share data)						
Balance at January 1, 2000	12,939,215	$1,984	$59,306	$(47,051)	$(53)	$(5,119)	$ 9,067
Issuance of ordinary shares at €3.94 ($3.79) per share	3,212,500	377	6,252	—	—	—	6,629
Issuance of 5,654,000 warrants at €0.00 per warrant	—	—	5,544	—	—	—	5,544
Issuance of 120,000 warrants at €0.00 per warrant	—	—	—	—	—	—	—
Exercise of options at €2.82 ($2.74) per share	20,000	2	53	—	—	—	55
Exercise of warrants at €0.12 ($0.12) per share	19,250	2	—	—	—	—	2
Exercise of warrants at €0.12 ($0.11) per share	6,625	1	—	—	—	—	1
Stock compensation	—	—	22	—	(22)	—	—
Amortization of deferred compensation	—	—	—	—	20	—	20
Net loss	—	—	—	(9,461)	—	—	(9,461)
Other compensation loss							
Translation adjustment	—	—	—	—	—	(975)	(975)
Comprehensive loss							(10,436)
Balance at December 31, 2000	16,197,590	$2,366	$71,177	$(56,512)	$(55)	$(6,094)	$ 10,882
Issuance of 70,000 warrants at €0.00 per warrant	—	—	—	—	—	—	—
Amortization of deferred compensation	—	—	—	—	23	—	23
Net loss	—	—	—	(2,874)	—	—	(2,874)
Other comprehensive loss							
Translation adjustment	—	—	—	—	—	(522)	(522)
Comprehensive loss							(3,396)
Balance at December 31, 2001	16,197,590	$2,366	$71,177	$(59,386)	$(32)	$(6,616)	$ 7,509
Issuance of 80,000 warrants at €0.01 per warrant	—	—	1	—	—	—	1
Issuance of 40,000 warrants at €0.01 per warrant	—	—	—	—	—	—	—
Amortization of deferred compensation	—	—	—	—	18	—	18
Net profit	—	—	—	3,005	—	—	3,005
Other comprehensive income							
Translation adjustment	—	—	—	—	—	1,753	1,753
Comprehensive income							4,758
Balance at December 31, 2002	16,197,590	$2,366	$71,178	$(56,381)	$(14)	$(4,863)	12,286

See notes to consolidated financial statements.

FLAMEL TECHNOLOGIES S.A.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31,		
	2000	2001	2002
	(Amounts in thousands of dollars)		
Cash flows from operating activities:			
Net income (loss)	$ (9,461)	$ (2,874)	$ 3,005
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Depreciation of property and equipment	1,082	1,270	1,460
Amortization of goodwill and other depreciation	31	—	—
Stock compensation expense	20	23	18
Increase (decrease) in cash from			
Accounts receivable	(1,139)	(5,184)	5,021
Inventory	(682)	251	271
Prepaid expenses and other current assets	264	78	37
Deferred revenue	3,012	1,089	(845)
Accounts payable	132	(259)	(101)
Accrued expenses	1,050	1,179	(1,429)
Research and development tax credit receivable	36	1,568	938
Other long-term assets and liabilities	33	75	396
Net cash provided by (used in) operating activities	(5,622)	(2,784)	8,771
Cash flows from investing activities:			
Purchases of property and equipment	(737)	(1,178)	(1,435)
Proceeds from disposal of property and equipment	—	3	3
Net cash used in investing activities	(737)	(1,175)	(1,432)
Cash flows from financing activities:			
Repayment of loans or advances	(7)	(110)	—
Proceeds from loans or capital leases	205	330	860
Principal payments on capital lease obligations	(305)	(416)	(459)
Cash proceeds from sale of ordinary shares and warrants	11,728	—	1
Net cash provided by (used in) financing activities	11,621	(196)	402
Effect of exchange rate changes on cash and cash equivalents	(335)	(673)	1,477
Net increase (decrease) in cash and cash equivalents	4,927	(4,828)	9,218
Cash and cash equivalents, beginning of year	5,210	10,137	5,309
Cash and cash equivalents, end of year	10,137	5,309	14,527
Supplemental disclosures of cash flow information:			
Capital lease obligations incurred	127	305	236

See notes to consolidated financial statements.

FLAMEL TECHNOLOGIES S.A.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business and Summary of Significant Accounting Policies

1.1. Nature of business

Flamel Technologies, S.A. (the "Company") is organized as a *Société Anonyme* or limited liability corporation under the laws of The Republic of France. The Company was founded in 1990. The Company is engaged in the development of advanced polymer technologies for unique life science applications. The Company operates primarily in France.

1.2. Principles of consolidation

The accompanying consolidated financial statements were prepared in accordance with accounting principles generally accepted in the United States (US GAAP).

The preparation of consolidated financial statements in conformity with US GAAP requires management to make estimates and assumptions that effect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

The accompanying consolidated financial statements include the Company and its wholly-owned subsidiary in the United States. All inter-company accounts and transactions have been eliminated.

1.3. Translation of financial statements of foreign entities

The reporting currency of the Company and its wholly-owned subsidiary is the U.S. dollar. All assets and liabilities in the balance sheets of the Company, whose functional currency is the Euro, are translated into U.S. dollar equivalents at exchange rates as follows: (1) asset and liability accounts at year-end rates; (2) income statement accounts at weighted average exchange rates for the year; and (3) shareholders' equity accounts at historical rates. Corresponding translation gains or losses are recorded in shareholders' equity.

Transaction gains and losses are reflected in the statement of operations. The Company has not undertaken hedging transactions to cover its currency translation exposure.

1.4. Revenue recognition and change in accounting principle

Research and laboratory analysis services revenue is recognized on a basis consistent with the performance requirements of the contracts. Certain fees payable to the Company under these contracts are milestone-related and are due in accordance with the terms of each contract when the milestone is achieved. The Company recognizes these milestone-related revenues only when each milestone has been fully performed, as agreed by the parties. Costs incurred under these contracts are considered costs in the period incurred. Payments received in advance of performance are recorded as deferred revenue and recognized on a systematic and rational basis to match the revenues with the related costs.

The Company recognizes revenue from unconditional grants received from governmental agencies in the period granted. Revenue from conditional grants received are recognized when all conditions stated in the grant have been met.

The Company recognizes revenue from product sales when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed and determinable, and collectibility is reasonably assured.

The Company has historically recognized non-refundable technology access fees received from its collaboration agreements as revenue when received. In December 1999, the Securities and Exchange Commission ("SEC") issued Staff Accounting Bulletin ("SAB") No. 101, "Revenue Recognition in Financial Statements." Among other things, SAB No. 101 describes the SEC staff's position on the

recognition of certain non-refundable up-front fees received in connection with research collaborations. The Company has evaluated the applicability of SAB No. 101 in conjunction with its existing collaborative agreements. As a result, effective January 1, 2000, the Company changed its method of accounting for the receipt of such fees to recognize revenue over the term of the related development period. The Company recorded the cumulative effect of a change in accounting principle of ($4,577,000) in the results for the year ended December 31, 2000. For the years ended December 31, 2001 and December 31, 2000, the Company has recorded $2,812,000 and $1,508,000 of license and research revenue, which were included in the cumulative effect adjustment recorded on January 1, 2000.

1.5. Research and development costs

Research and development (R&D) expenses are comprised of the following types of costs incurred in performing R&D activities: salaries, allocated overhead and occupancy costs, clinical trial and related clinical manufacturing costs, contract and other outside service fees. R&D expenses consist of independent R&D costs and costs associated with collaborative R&D and in-licensing arrangements. Research and development expenditures are charged to operations as incurred.

1.6. Concentration of credit risk

The Company’s cash and cash equivalents are deposited with Crédit Lyonnais and Crédit Agricole, major French banks.

The Company’s revenues are derived mainly from collaborative research and development contracts with pharmaceutical and chemical companies based in Europe and the United States. All significant customers are discussed in Note 3.

The Company performs ongoing credit evaluations of its customers and maintains provisions for potential credit losses as considered necessary. The Company generally does not require collateral. Historically, the Company has not experienced significant credit losses on its customer accounts. At December 31, 2002 and December 31, 2001, there was no allowance for doubtful accounts recorded.

1.7. Net result per share

Basic earnings per share is computed by dividing income available to common shareholders by the weighted average number of shares of common stock outstanding for the period. Diluted earnings per share reflects potential dilution that could occur if securities or other contracts to issue common stock were exercised or converted into common stock or resulted in the issuance of common stock that then shared in the earnings of the Company. The dilutive effects of the Company’s common stock options and warrants is determined using the treasury stock method to measure the number of shares that are assumed to have been repurchased using the average market price during the period, which is converted from U.S. dollars at the average exchange rate for the period.

For the years ended December 31, 2000 and 2001, the effects of dilutive securities were excluded from the calculation of earnings per share as a net loss was reported in those periods.

1.8. Cash and cash equivalents

The Company considers all highly liquid investments purchased with an original maturity date of three months or less to be cash equivalents. Cash and cash equivalents consist of money market funds. All cash equivalents as of December 31, 2001 and 2002 are classified as available-for-sale securities in accordance with Statement of Financial Accounting Standards No. 115, “Accounting for Certain Investments in Debt and Equity Securities” (SFAS 115).

All available-for-sale securities are recorded at fair market value and unrealized gains and losses are included in accumulated other comprehensive income in shareholders' equity, net of related tax effects. Gross realized gains on sales of these available-for-sale securities amounted to $351,000, $278,000 and $252,000 for the years ended December 31, 2000, 2001 and 2002, respectively. Unrealized gains in each of the three years presented were not material.

1.9. Inventories

Inventories consist principally of raw materials and finished products, which are stated at the lower of cost (first-in, first-out) or market. The components of inventories were as follows:

	December 31,	
	2001	2002
	(In thousands of U.S. dollars)	
Raw materials	$249	$375
Finished goods	320	—
Inventories, net	569	375

1.10. Property and equipment

Property and equipment is stated at historical cost less accumulated depreciation. Depreciation and amortization are computed using principally the straight-line method over the estimated useful lives of three to twenty years. Assets under capital leases are amortized over the economic life of the asset or the remaining lease term, whichever is shorter. Amortization of capital leases is included in depreciation expense. The components of property and equipment were as follows:

	December 31,	
	2001	2002
	(In thousands of U.S. dollars)	
Land and buildings	$ 78	$ 93
Laboratory equipment	8,210	11,257
Office and computer equipment	771	970
Furniture and fixtures	1,984	2,537
Total property and equipment	11,043	14,857
Less accumulated depreciation and amortization	(8,371)	(11,452)
Property and equipment, net	2,672	3,405

1.11. Impairment of Long-Lived Assets

Property and equipment and other long-lived assets are reviewed for impairment whenever events or circumstances indicate that the carrying amount may not be recoverable. If undiscounted expected future cash flows are less than the carrying value of the assets, an impairment loss will be recognized based on the excess of the carrying amount over the fair value of the assets.

1.12. Income taxes

The Company accounts for income taxes in accordance with SFAS No. 109, "Accounting for Income Taxes" (SFAS 109). Under SFAS 109, deferred tax assets are determined based on the difference between the financial reporting and tax basis of assets and liabilities, applying enacted statutory tax rates in effect for the year in which the tax differences are expected to reverse. Deferred tax assets are reduced by a valuation

allowance when, in the opinion of management, it is more likely than not that some portion or all of the deferred tax assets will not be realized. Deferred tax assets and liabilities are adjusted for the effects of changes in the tax laws and rates on the date of enactment.

1.13. Employee stock option plans

At December 31, 2002, the Company has five stock-based employee compensation plans, which are described more fully in Note 5.4. The Company accounts for those plans under the recognition and measurement principles of APB Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25), and related Interpretations. In accordance with APB 25, the Company recognizes stock-based employee compensation cost over the vesting period when the options granted under those plans have an exercise price lower than the market value of the underlying common stock on the date of grant. The following table illustrates the effect on net income and earnings per share if the company had applied the fair value recognition provisions of FASB Statement No. 123, *Accounting for Stock-Based Compensation*, to stock-based employee compensation.

	December 31,		
	2000	2001	2002
	(In thousands of U.S. dollars)		
Net income (loss), as reported	$ (9,461)	$(2,874)	$ 3,005
Add: Stock-based employee compensation expense included in reported net income (loss), net of related tax effects	20	23	18
Deduct: Total stock-based employee compensation expense determined under fair value based method for all awards, net of related tax effects	(835)	(905)	(1,857)
Pro forma net income (loss)	(10,276)	(3,779)	1,166
Earnings per share			
Basic, as reported	(0.62)	(0.18)	0.19
Basic, pro forma	(0.67)	(0.23)	0.07
Diluted, as reported	(0.62)	(0.18)	0.18
Diluted, pro forma	(0.67)	(0.23)	0.07

The fair value of each stock option granted during the year is estimated on the date of grant using the Black-Scholes option pricing model with the following assumptions:

	Year Ended December 31,		
	2000	2001	2002
Weighted average expected life (years)	8	8	8
Expected volatility rates	100%	100.6%	91.07%
Expected dividend yield	—	—	—
Risk-free interest rate	5%	5%	4.25%
Weighted-average fair value of options granted during the year (in U.S. dollars)	4.39	1.42	2.15

1.14. Comprehensive Income

Other comprehensive income for the Company consists solely of translation adjustments and is shown separately in the consolidated statements of shareholders' equity.

1.15. New Accounting Pronouncements

In June 2001, the Financial Accounting Standards Board issued SFAS 143, "Accounting for Asset Retirement Obligations" (SFAS 143). SFAS 143 requires the fair value of a liability for an asset retirement obligation be recognized in the period in which it is incurred if a reasonable estimate of fair value can be made. The associated asset retirement costs are capitalized as part of the carrying amount of the long-lived asset. An entity shall measure changes in the liability for an asset retirement obligation due to passage of time by applying an interest method of allocation to the amount of the liability at the beginning of the period. That amount shall be recognized as an increase in the carrying amount of the liability and as an expense classified as an operating item in the statement of income. SFAS 143 will become effective for Flamel Technologies beginning on January 1, 2003. Flamel Technologies does not expect that adoption of SFAS 143 will have a material impact on its financial position, results of operations or cash flows.

In June 2002, the Financial Accounting Standards Board issued SFAS No. 146, "Accounting for Costs Associated with Exit or Disposal Activities" (SFAS 146). The Statement requires companies to recognize costs associated with exit or disposal activities when they are incurred rather than at the date of a commitment to an exit or disposal plan. The Statement replaces EITF Issue No. 94-3, "Liability Recognition for Certain Employee Termination Benefits and Other Costs to Exit an Activity (including Certain Costs Incurred in a Restructuring)." The Company is required to apply this Statement prospectively to exit or disposal activities initiated after December 31, 2002, with earlier application encouraged. The Company does not expect that adoption of SFAS 146 will have a material impact on its financial position, results of operations or cash flows.

On November 25, 2002, the Financial Accounting Standards Board announced the issuance of Interpretation No. 45, "Guarantor's Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others," which expands on the accounting guidance of Statements No. 5, 57, and 107 and incorporates without change the provisions of FASB Interpretation No. 34, which has been superseded by this Interpretation. Given observed differences in practice, this Interpretation clarifies the requirements for a guarantor's accounting and interim and annual financial statement disclosures of certain guarantees issued and outstanding. It also clarifies that a guarantor is required to recognize, at the inception of a guarantee, a liability for the fair value of the obligation undertaken in issuing the guarantee. This Interpretation does not prescribe a specific approach for subsequently measuring the guarantor's recognized liability over the term of the related guarantee. The incremental disclosure requirements in this Interpretation are effective for financial statements of interim or annual periods ending after December 15, 2002. The initial recognition and initial measurement provisions of this Interpretation are applicable to guarantees issued or modified after December 31, 2002. Flamel Technologies is currently reviewing this interpretation to measure the potential impact on its results of operations and financial position.

In November 2002, the EITF reached a consensus on issue No. 00-21 *Accounting for Revenue Arrangements with Multiple Deliverables* ("EITF 00-21") on a model to be used to determine when a revenue arrangement involving the delivery or performance of multiple products, services and/or rights to use assets should be divided into separate units of accounting. Additionally, EITF 00-21 addresses if separation is appropriate, how the arrangement consideration should be allocated to the identified accounting units. EITF 00-21 will be applicable to agreements entered into in fiscal periods beginning after June 15, 2003, with early adoption permitted. In addition, companies are permitted to apply EITF 00-21 to all existing arrangements as the cumulative effect of a change in accounting principle in accordance with APB Opinion No. 20, *Accounting Changes*. The Company will adopt EITF 00-21 for revenue arrangements that are initiated after January 1, 2004 and is currently assessing what the impact of EITF 00-21 will be on its financial statements.

In December 2002, the Financial Accounting Standards Board issued FASB Statement No. 148, "Accounting for Stock-Based Compensation — Transition and Disclosure" ("SFAS 148"). This Statement amends FASB Statement No. 123, "Accounting for Stock-Based Compensation" ("SFAS 123"), to provide

alternative methods of transition to SFAS 123's fair value method of accounting for stock-based employee compensation. It also amends the disclosure provisions of SFAS 123 to require prominent disclosure in the summary of significant account policies of the effects of an entity's accounting policy with respect to stock-based employee compensation on reported net income and earnings per share in annual financial statements. SFAS 148's amendment of the transition and annual disclosure requirements are effective for fiscal years ending after December 15, 2002. Refer to Note 1.13 for disclosures related to stock based compensation. The Company intends to continue to account for stock-based compensation based on the provisions of APB Opinion No. 25.

2. Subcontracting Agreement

In accordance with the terms of a subcontracting agreement signed with SmithKline in December 1996, the Company realized, from its pharmaceutical production facility based in Pessac (near Bordeaux, France), sales mainly of cimetidine formulations to SmithKline for a total amount of $1,167,000 in 2000 and $322,000 in 2001. This agreement was renewed for 2002 and the sales to SmithKline totaled $121,000.

3. License, Research and Consulting Agreements

Novo Nordisk

In December 1999, the Company signed a development and licensing agreement with Novo Nordisk for Flamel's Basulin® long-acting basal insulin product. Pursuant to the terms of the agreement, Flamel received licensing fees, regular research payments, and potentially milestones and royalties on future product sales and Novo Nordisk acquired, during the term of the agreement world wide development and marketing rights to Basulin®.

As part of the agreement, the Company received a $5,000,000 licensing fee in December 1999, which was recorded as revenue in 1999. However, effective January 1, 2000, due to the change of the method of accounting for the receipt of such fees, as described in Note 1.5, the Company recorded the cumulative effect of a change in accounting principle of ($4,577,000) in the statement of operations for the year ended December 31, 2000.

In 2000, the Company recognized research and development revenues of $2,760,000 and licensing fees of $1,565,000 in accordance with the new accounting principle.

In December 2001, Novo Nordisk gave notice of the termination of the license agreement with Flamel, effective as of March 12, 2002. The Company has fulfilled all of its substantive obligations under this contract as of December 31, 2001 and recognized research and development revenues of $2,971,000 and $595,000 in 2001 and 2002, respectively, and licensing fees of $2,812,000 in 2001.

Corning

In December 1998, the Company signed a long-term research and product development agreement with Corning France and Corning Incorporated. This agreement is an expansion of the research agreement that had existed between Flamel and Corning from January 1994 to January 1998 for the co-development of proprietary new material to be incorporated in the manufacturing of ophthalmic and sunglasses lenses. Pursuant to the terms of this agreement, Flamel receives regular research payments and royalties on the sales of Corning products that utilize Flamel's innovations. In relation to this agreement, the Company recognized research revenue and sales of pilot batches of $858,000, $870,000 and $757,000 in 2000, 2001 and 2002, respectively.

The Company realized sales of specialty material for ophthalmic lenses of $1,447,000 in 2000, $651,000 in 2001 and $539,000 in 2002 and recognized royalties on Corning's sales of $1,055,000 in 2000, $961,000 in 2001 and $895,000 in 2002.

G.D. Searle & Co

In January 1996, the Company entered into an agreement with G.D. Searle & Co. ("Searle") giving the latter exclusive rights to market the Company's Asacard™ product in all countries of Western Europe with the exception of Belgium, the Netherlands, Luxembourg, and potentially France. An agreement was signed with Searle in September 2000 to terminate the contract. The Company recognized of revenue of $500,000 in 2000, which represented the fee received for the termination of the contract.

Ministry of Research and Technology

In June 1998, the Company was granted a non-refundable subsidy from the French Ministry of Research and Technology for a research project related to the development of an oral insulin. The Company received payments representing 50% of the total expenses incurred on this project over a three-year period. Total expenses for the project were estimated at $2,287,000. In accordance with the contract and expenses incurred, the Company recognized revenues of $248,000 in 2000 and $200,000 in 2001. This contract expired in December 2001.

Servier

In December 2001, Flamel Technologies and Laboratoires Servier ("Servier") entered into a license and development agreement whereby the Company agreed to license its Micropump® control release technology to Servier for use with an undisclosed product of Servier. In consideration for the agreement, Servier agreed to make a $3 million initial payment and additional milestone payments upon achievement of certain events. The $3,000,000 initial payment has been recognized on a straight-line basis over the term of the license agreement *(i.e.* 3 years). The Company recognized licensing fees of $42,000 in 2001 and $955,000 in 2002 with respect to this initial payment. In addition, Flamel recognized two milestone payments of $1.5 million and $4 million as licensing revenue in 2002. Flamel also recognized research and development revenues of $2,339,000 in 2002.

Beecham Pharmaceuticals

In June 2002, Flamel Technologies entered into a license agreement with Beecham Pharmaceuticals (Pte) Limited, ("Beecham") whereby the Company agreed to license its controlled-release Micropump technology to Beecham in connection with the sachet formulation of its drug Augmentin®. In consideration for the license, Beecham agreed to make an upfront payment of $1.5 million, additional milestone payments upon achievement of certain events and royalty payments on sale of the product. The $1,500,000 upfront payment has been recognized on a straight-line basis over the term of the license agreement (*i.e.* 3 years). The Company recognized licensing fees of $168,000 in 2002 with respect to this upfront payment. In 2002, Flamel also recognized a $1.5 million milestone payment as licensing fees, and research and development revenues of $123,000.

Others

The Company recognized research and development revenues on seven feasibility studies with undisclosed partners for an amount of $2,968,000 in 2001 and $2,776,000 in 2002. Such revenues were not material in 2000.

4. Long-Term Debt

Long-term debt comprises:

	December 31,	
	2001	2002
	(In thousands of U.S. dollars)	
Anvar loans:		
Asacard program	$ 604	$ 719
Other programs	175	208
Grants from Datar and other agencies	391	693
French Ministry of Industry	—	464
Total	1,170	2,084
Current portion	391	693
Long-term portion	779	1,391

Anvar is an agency of the French government that provides financing to French companies for research and development. At December 31, 2001 and 2002, the Company had outstanding loans from Anvar of $779,000 and $927,000, respectively. These loans do not bear interest and are repayable only in the event the research project is technically or commercially successful. In 2001, the Company renegotiated the timing for the potential repayment of those loans, which was initially scheduled between 2002 and 2005. Potential repayment is now scheduled to occur from 2005 through 2008.

The Company also recorded in 2001 an income of $219,000 related to the abandonment by Anvar of its loan on the Collagene research project due to commercial failure. This abandonment is subject to a clause of return to profitability (see Note 9.3).

At December 31, 2001 and 2002, the Company had also recorded obligations of $391,000 and $693,000, respectively, related to conditional grants from Datar and other French public agencies. These grants are linked to investments in the development of the Pessac facility from June 1997 to June 2002, under which the Company can receive up to $1,038,000. Future grants and other subsidies are subject to the achievement before the end of June 2002 of the investment and employment objectives described in the development plan of the plant submitted to those public agencies. In the event that those objectives are not realized in the time frame specified, there is the risk of a partial or total reimbursement of the amounts received by the Company. The Company has not received any notification so far.

The payments received between 1999 and 2002 have been accounted for as advances and, accordingly have not been included in revenues.

In 2002, the Company also received a grant of $464,000 from the French Ministry of Industry on a research project (the “Proteozome” project) related to the development of new Medusa® applications. Pursuant to the agreement, the Company will be granted a total amount representing 50% of the total expenses incurred on this project over a three-year period beginning on January 2, 2002. Total expenses for the project are estimated at $3,093,000. This loan will be repaid for one third in July 2008 and for two thirds in July 2011, and is not bearing interest.

Future payments on long-term debt for the years ending December 31 (assuming the underlying project is commercially or technically successful for governmental research loans, but without considering possible

success-based payment on the Collagene project, and assuming no reimbursement of grants from Datar and other agencies) are as follows:

	December 31,
	(In thousands of U.S. dollars)
2005	$ 168
2006	232
2007	287
2008	704
	$1,391

5. Shareholders' Equity

5.1. General

At December 31, 2002, the issued and outstanding share capital of the Company consists of 16,197,590 ordinary shares, nominal value €0.13 per share.

On February 29, 2000, as a result of an exercise of stock options, the Company issued 20,000 ordinary shares at a price of €2.82 ($2.74) per share.

On March 24, 2000, as a result of the exercise of warrants by shareholders, the Company issued 19,250 ordinary shares at a price of €0.13 ($0.12) per share.

On April 6, 2000, the Company issued 3,212,500 ordinary shares at €3.94 (approximately $3.79) to certain private investors, including the venture capital funds and affiliates of Biotechnology Value Fund, Alta Partners and Chase Capital Partners. In addition, the Company issued warrants at a price of €0.00 (FRF0.01) per warrant to purchase up to 3,726,750 ordinary shares to these same investors (see Note 5.3). These warrants provide for physical settlement in unregistered shares and convey no other rights. Total proceeds from this issuance amounted to $12.2 million. The proceeds have been allocated to additional paid-in capital on common stock and warrants based on the respective relative fair values at the time of issuance.

On June 4, 2000, as a result of the exercise of warrants by shareholders, the Company issued 6,625 ordinary shares at a price of €0.13 ($0.12).

Shareholders have preemptive rights to subscribe for additional shares issued by the Company for cash on a *pro rata* basis.

Shareholders may waive such preemptive subscription rights at an extraordinary general meeting of shareholders under certain circumstances.

Preemptive subscription rights, if not previously waived, are transferable during the subscription period relating to a particular offer of shares.

5.2. Dividends

The Company has no plans to distribute dividends in the foreseeable future.

5.3. Warrants

On April 6, 2000, the Company issued warrants at a price of €0.00 (FRF0.01) per warrant to purchase up to 3,726,500 ordinary shares to certain private investors, including the venture capital funds and affiliates of Biotechnology Value Fund, Alta Partners and Chase Capital Partners. These warrants provide for physical

settlement in unregistered shares and convey no other rights. This issuance included 1,799,000 Class A warrants, 1,927,500 Class B warrants and 1,927,500 Class C warrants. These warrants have a five-year term. The Class A warrants are exercisable at €5.96 (approximately $6.00) per share, the Class B warrants are exercisable at €5.96 (approximately $6.00) per share and the Class C warrants are exercisable at €0.13 (approximately $0.12) per share. The number of Class B Warrants and Class C warrants that may be exercised has been determined in relation to the closing price of the Company's ADSs on the Nasdaq National Market in 2000. Based on the stock closing price during the year 2000, 1,285,000 Class C warrants, and 642,500 Class B warrants are exercisable at December 31, 2001 and expire in March 2005.

On June 14, 2000 the Company issued at a price of €0.00 (FRF0.01) per warrant, 120,000 warrants, giving the right to subscribe for 120,000 ordinary shares at the price of €4.88 ($4.31) per share to certain Directors of the Company. These warrants are issued for a five-year period and will vest over four years from the date of issuance. At December 31, 2002, 80,000 of those warrants remain exercisable, subject to the vesting provisions.

On July 19, 2001 the Company issued at a price of €0.00 (FRF0.01) per warrant, 70,000 warrants, giving the right to subscribe for 70,000 ordinary shares at the price of €5.95 ($5.25) per share to certain Directors of the Company. These warrants are issued for a five-year period and will vest over four years from the date of issuance. At December 31, 2002, 20,000 of those warrants remain exercisable, subject to the vesting provisions.

On June 20, 2002 the Company issued at a price of €0.01 per warrant, 80,000 warrants, giving the right to subscribe for 80,000 ordinary shares at the price of €2.33 per share to certain Directors of the Company. These warrants are issued for a five-year period and will vest over four years from the date of issuance. At December 31, 2002, 80,000 of those warrants remain exercisable, subject to the vesting provisions.

On September 19, 2002 the Company issued at a price of €0.01 per warrant, 40,000 warrants, giving the right to subscribe for 40,000 ordinary shares at the price of €1.36 per share to a Director of the Company. These warrants are issued for a five-year period and will vest over four years from the date of issuance. At December 31, 2002, 40,000 of those warrants remain exercisable, subject to the vesting provisions.

5.4. Stock options

The Company has issued stock options under plans approved by shareholders in 1990, 1993, 1996, 2000 and 2001. Generally, each option vests ratably over a four-year period from the date of grant. The difference between the exercise price and the fair value of the underlying share on the grant date has been recorded as deferred compensation expense and is being amortized over the vesting period. The amounts expensed under these plans in 2000, 2001 and 2002 were $20,000, $23,000 and $18,000, respectively.

The activity under the option plans were as follows:

	Shares Available for Grant	Options Outstanding	Weighted Average Exercise Price($)
Balance at January 1, 2000	430,000	570,000	4.19
Options Issued	1,000,000	—	—
Granted	(1,025,000)	1,025,000	5.40
Exercised	—	(20,000)	2.64
Cancelled or expired	280,000	(280,000)	3.90
Balance at December 31, 2000	685,000	1,295,000	5.23
Options Issued	750,000		
Granted	(960,000)	960,000	1.64
Cancelled or expired	45,000	(245,000)	4.53
Balance at December 31, 2001	520,000	2,010,000	3.63
Options Issued	—	—	—
Granted	(695,000)	695,000	2.73
Cancelled or expired	290,000	(390,000)	3.64
Balance at December 31, 2002	115,000	2,315,000	3.36

Stock options outstanding at December 31, 2002, which expire from 2007 to 2012, had exercise prices ranging from €1.09 to €7.58. The weighted average remaining contractual life of all options is 8 years.

The effects of applying the fair value method provided under SFAS No. 123 are shown in Note 1.13 and are not necessarily indicative of future amounts.

In January 1997, the French parliament adopted a law that requires French companies to pay social contributions, which generally represent 45% of the taxable salary, on the difference between the exercise price of a stock option and the fair market value of the underlying shares on the exercise date if the beneficiary sells the stock before a five-year period following the grant of the option. The new law is consistent with personal income tax law that requires individuals to pay income tax on the difference between the option exercise price and the fair value of the shares at the grant date if the shares are sold within five years of the option grant. The law applies to all options exercised after January 1, 1997.

The Company has not recorded a liability for social charges which may be assessed for options granted in 2001 and 2002 as the liability, which is dependent on future trading values of the Company's shares and the timing of employees decisions to exercise options and sell the related shares, cannot be estimated. The Company also does not consider that the liability is probable due to the income tax disincentives to employees of exercising options and selling the shares in less than a five-year period.

6. Income Taxes

Income (loss) before income taxes is comprised of the following:

	December 31,		
	2000	2001	2002
	(In thousands of U.S. dollars)		
France	$(9,411)	$(2,860)	$2,452

The Company was not eligible for the research and development tax credit in 2000 and 2001 due to the limited increase of research and development expenses in 2000 and 2001 as compared to 1998, 1999 and

2000, respectively. The income tax benefit in 2002 amounted to $564,000 and was principally related to the research and development tax credit recorded in France.

Research and development credits are recoverable in cash in the fourth year after the credit is earned, if the credit has not been applied against taxes payable. Income tax expense amounted to $50,000 in 2000 and represents the $16,000 minimum income tax payable in France and a $34,000 adjustment to the research and development tax credits from prior years following the conclusions of a tax audit. Income tax expense amounted to $14,000 in 2001 and represents the minimum income tax payable in France.

A reconciliation of income tax benefit computed at the French statutory rate (36.6% in 2000, 35,4% in 2001 and 34.4% in 2002) to the income tax benefit is as follows:

	December 31,		
	2000	2001	2002
	(In thousands of U.S. dollars)		
Income tax benefit (provision) computed at the French statutory rate	$ 3,444	$ 1,010	$(843)
Operating losses not utilized	(3,444)	(1,010)	843
Research credits	(34)	—	567
Minimum tax payable	(16)	(14)	(14)
Total	$ (50)	$ (14)	$ 553

Significant components of the Company's deferred taxes consist of the following:

	Year December 31,	
	2001	2002
	(In thousands of U.S. dollars)	
Deferred tax assets:		
Net operating loss carry-forwards	$ 10,403	$ 10,450
Other deferred tax assets	32	52
Deferred tax liabilities	—	—
Net deferred tax assets	10,435	10,502
Valuation allowance	(10,435)	(10,502)
Deferred taxes, net	$ —	$ —

The Company has provided valuation allowances covering 100% of net deferred tax assets due to the Company's history of losses.

As of December 31, 2002, the Company has $30,381,000 in French net operating loss carry-forwards of which $9,367,000 has no expiration date. The remaining carry-forwards expire as follows:

December 31,	(In thousands of U.S. dollars)
2003	$ 7,515
2004	4,962
2005	6,645
2006	1,892
	$21,014

The Company was subject to an income tax audit in 1999 covering various tax items for periods extending from 1995 through April 30, 1999. The Company came to an agreement with Fiscal Administration

concerning research tax credit and recorded an adjustment of $34,000 to research tax credit receivables. The research tax credit receivable to the Company is expected to be received in accordance with the following timetable:

December 31,	(In thousands of U.S. dollars)
2003	$260
2007	630
Total	$890

7. Employee Retirement Plans

In accordance with French law, post-retirement and post-employment benefits for most of the Company's employees are sponsored by the relevant government agencies in France. The Company's liability with respect to these plans is mostly limited to specific payroll deductions. There is no further liability in connection with these plans.

French law also requires payment of a lump sum retirement indemnity to all employees based upon years of service and compensation at retirement. Benefits do not vest prior to retirement. There is no formal plan and no funding of the obligation is required. The provision has been calculated taking into account the estimated payment at retirement (discounted to the current date), turnover and salary increases. As of December 31, 2001 and 2002, the liability for retirement indemnities amounted to $249,000 and $414,000, respectively.

In the United States, the Company sponsors a defined contribution plan. During 2000, 2001 and 2002, the Company made contributions of approximately $52,000, $11,000 and $35,000 to the plan, respectively.

8. Fair Value of Financial Instruments

At December 31, 2001 and 2002, the carrying values of financial instruments such as cash and cash equivalents, trade receivables and payables, other receivables and accrued liabilities and the current portion of long-term debt approximated their market values, based on the short-term maturities of these instruments.

At December 31, 2001 and 2002, the fair value of long-term debt with carrying value of $779,000 and $1,391,000, was estimated to be $614,000 and $1,086,000, respectively. Fair value was determined based on expected future cash flows, discounted at market interest rates.

9. Commitments and Contingencies

9.1. Capital leases

The Company leases certain of its equipment under capital leases. Capitalized costs of $2,356,000 and $3,064,000 are included in property and equipment at December 31, 2001 and 2002. Accumulated amortization of these leased assets was approximately $1,714,000 and $2,586,000 at December 31, 2001 and 2002, respectively.

Future payments on capital leases for the years ending December 31 are as follows:

December 31,	(In thousands of U.S. dollars)
2003	$ 249
2004	150
2005	13
Total	412
Less amounts representing interest	(34)
Capital lease	378
Less current portion	(229)
Long-term portion	$ 149

Interest paid in the years ended December 31, 2000, 2001 and 2002 was approximately $48,000, $50,000 and $46,000, respectively. Depreciation expense on assets held under capital leases is included in total depreciation expense for the years ended December 31, 2000, 2001 and 2002 and amounted to $298,000, $385,000 and $493,000, respectively.

9.2. Operating leases

The Company leases its facilities and certain equipment under operating leases which expire through 2006. Future minimum lease payments under operating leases due for the fiscal years ending December 31 are as follows:

December 31,	(In thousands of U.S. dollars)
2003	$290
2004	268
2005	202
2006	26

Rental expense for the years ended December 31, 2000, 2001 and 2002 was approximately $349,000, $451,000, and $418,000, respectively.

9.3. Other commitments

The Company recorded in 2001 an income of $219,000 related to the abandonment by Anvar of its loan on the Collagene research project due to commercial failure (see Note 5). This abandonment is subject to a clause of return to profitability. Pursuant to the clause, the Company agreed to reimburse the Anvar every year an amount representing 4% of the related products sales, if any, in the limit of $219,000. The clause is effective for a 9-year period beginning as of November 2001.

9.4. Gain contingencies

In 2002, the Company recognized revenue of $2,526,000 as the final result of the litigation with the Wellcome Foundation on Genvir™ after the signature in January 2002 of a final settlement on that procedure. Such revenue is classified in other income in the statements of operations for the year ended December 31, 2002.

9.5. Litigations

The Company is involved in a number of claims and lawsuits considered normal in its business, including employee litigations. While it is not possible to predict the outcome of legal actions brought against the Company, the Company believes that the liability resulting from the pending claims and suits would not have a material adverse effect on the results of its operations, cash flows, or financial position as of December 31, 2002, and for the year then ended.

10. Industry and Geographic Information

The Company operates in one segment, the development and commercialization of controlled-release therapeutic products based on its proprietary polymer based technology.

Operations outside of France consist principally of the operations of the U.S. subsidiary, which had no sales to third parties in 2000, 2001 or 2002.

Revenues generated from customers outside of France (export sales) amounted to $5,265,000, $7,733,000 and $6,358,000 in 2000, 2001 and 2002, respectively.

FLAMEL TECHNOLOGIES S.A.

CONDENSED CONSOLIDATED BALANCE SHEET (UNAUDITED)

	June 30, 2003
	(Amounts in thousands of dollars)
ASSETS	
Current assets:	
Cash and cash equivalents	$ 11,649
Accounts receivable	6,008
Inventory	1,069
Prepaid expenses and other current assets	936
Total current assets	19,662
Property and equipment, net	3,431
Other assets:	
Research and development tax credit receivable	686
Other long-term assets	77
Total other assets	763
Total assets	$ 23,856
LIABILITIES AND SHAREHOLDERS' EQUITY	
Current liabilities:	
Current portion of long-term debt	$ 99
Current portion of capital lease obligations	190
Accounts payable	2,388
Current portion of deferred revenue	2,826
Accrued expenses	1,897
Advances from customers	284
Other current liabilities	112
Total current liabilities	7,796
Long-term debt, less current portion	1,516
Other long-term liabilities	1,144
Deferred revenue, less current portion	2,678
Capital lease obligation, less current portion	81
Total long-term liabilities	5,419
Shareholders' equity:	
Ordinary shares	2,384
Additional paid-in capital	71,854
Accumulated deficit	(59,704)
Deferred compensation	(10)
Cumulative other comprehensive loss	(3,883)
Total shareholders' equity	10,641
Total liabilities and shareholders' equity	$ 23,856

See notes to unaudited condensed consolidated financial statements.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS (UNAUDITED)

(Amounts in thousands of dollars except share data)

	Six months ended June 30,	
	2002	**2003**
Revenue:		
License and research revenue	$ 5,360	$ 6,259
Product sales and services	1,314	1,901
Other revenue	535	372
Total revenue	7,209	8,532
Costs and expenses:		
Cost of goods and services sold	(1,081)	(1,811)
Research and development	(5,695)	(8,525)
Selling, general and administrative	(1,791)	(2,351)
Stock compensation expense	(10)	(4)
Total costs and expenses	(8,577)	(12,691)
Loss from operations	(1,368)	(4,159)
Other income	2,396	1,007
Interest income, net	78	142
Foreign exchange loss	(147)	(293)
Income tax expense	—	(21)
Net income (loss)	$ 959	$ (3,324)
Earnings (loss) per ordinary share		
Basic	$ 0.06	$ (0.20)
Diluted	0.06	(0.20)
Weighted average number of ordinary shares outstanding (in thousands)		
Basic	16,198	16,327
Diluted	16,711	16,327

FLAMEL TECHNOLOGIES S.A.

CONDENSED CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY (UNAUDITED)

(Amounts in thousands of dollars except share data)

	Ordinary Shares		Additional Paid-in Capital	Accumulated Deficit	Deferred Compensation	Cumulative Translation Adjustment	Shareholders' Equity
	Shares	Amount					
				(Amounts in thousands of dollars except per share data)			
Balance January 1, 2003	16,197,590	$2,366	$71,178	$(56,381)	$(14)	$(4,863)	$12,286
Issuance of ordinary shares at €4.75 ($5.50)	82,000	12	439				451
Issuance of ordinary shares at €2.78 ($3.21)	2,500		8				8
Issuance of ordinary shares at €4.88 ($5.76)	30,000	4	169				173
Issuance of ordinary shares at €5.95 ($7.02)	5,000	1	34				35
Issuance of ordinary shares at €2.33 ($2.75)	10,000	1	26				27
Amortization of deferred compensation	—	—	—	—	4	—	4
Net loss	—	—	—	(3,323)	—	—	(3,323)
Other comprehensive income							
Translation adjustment	—	—	—	—	—	980	980
Comprehensive income							(2,343)
Balance June 30, 2003	16,327,090	$2,384	$71,854	$(59,704)	$(10)	$(3,883)	$10,641

See notes to unaudited condensed consolidated financial statements.

FLAMEL TECHNOLOGIES S.A.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS (UNAUDITED)

(Amounts in thousands of dollars)

	Six months ended June 30,	
	2002	**2003**
Cash flows from operating activities:		
Net income (loss)	$ 959	$ (3,323)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities :		
Depreciation	619	604
Stock compensation expense	10	4
(Gain) loss on disposal of property and equipment		(362)
(Gain) loss on recognition of grants		(769)
Increase (decrease) in cash from:		
Accounts receivable	4,596	(2,162)
Inventory	400	(638)
Prepaid expenses and other current assets	(75)	(542)
Deferred revenue	(23)	1,363
Accounts payable	(48)	916
Accrued expenses	(1,616)	(375)
Research and development tax credit receivable	1,416	274
Other	109	138
Net cash provided by (used in) operating activities	6,346	(4,872)
Cash flows from investing activities:		
Purchases of property and equipment	(817)	(368)
Proceeds from disposal of property and equipment		372
Net cash provided by (used in) investing activities	(817)	4
Cash flows from financing activities:		
Proceeds from loans	—	135
Cash proceeds from sale of ordinary shares	—	694
Principal payments on loans and capital lease obligations	(212)	(126)
Net cash provided by (used in) financing activities	(212)	703
Effect of exchange rate changes on cash and cash equivalents	1,280	1,294
Net increase (decrease) in cash and cash equivalents	6,597	(2,871)
Cash and cash equivalents, beginning of period	5,309	14,527
Cash and cash equivalents, end of period	$11,906	$11,649

See notes to unaudited condensed consolidated financial statements.

1. Summary of Significant Accounting Policies

In the opinion of management, the accompanying unaudited condensed consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States for interim financial statements. Accordingly, they do not include all of the information and footnotes required by accounting principles generally accepted in the United States (US GAAP) for complete financial statements. In the opinion of management, all adjustments (consisting of only normal recurring accruals) considered necessary for a fair presentation have been included.

The preparation of consolidated financial statements in conformity with USGAAP requires management to make estimates and assumptions that effect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Operating results for the six months ended June 30, 2003 are not necessarily indicative of the results that may be expected for the year ending December 31, 2003. These condensed consolidated financial statements should be read in conjunction with the Company's audited annual financial statements.

2. Revenues

2.1 License research and consulting agreements.

In accordance with the long-term research and product development agreement signed with Corning in December 1998, the Company recognized research and development revenues of $192,000 for the first six months of 2003.

In accordance with the license agreement signed with Servier in December 2001, the Company recognized research and development revenues of $895,000 and licensing fees of $1,100,000 for the first six months of 2003. The licensing fees include a milestone payment of $427,000 related to results achieved in June 2003.

In accordance with the license agreement signed with Beecham Pharmaceuticals (Pte) Limited in June 2002, the Company recognized licensing fees of $281,000 for the first 2003 semester.

In accordance with the license agreement signed with SB Pharma Purto Rico Inc. in March 2003, the Company recognized research and development revenues of $1,584,000 and licensing fees of $1,114,000 for the first six months of 2003. The licensing fees include a milestone payment for $943,000 for results achieved in June 2003. The remaining $171,000 relates to the $2,000,000 upfront payment received in March 2003 and recognized as revenue on a straight-line basis over the term of the development period.

In accordance with the license agreement signed with Biovail in February 2003, the Company recognized revenue of $47,000 in the six-month period ended June 2003 relating to the $500,000 upfront payment received in February 2003.

The Company recognized research and development revenues on three feasibility studies with undisclosed partners for an amount of $989,000 for the first six months of 2003.

2.2 Other revenues.

In accordance with the long-term research and product development agreement signed with Corning in December 1998, the Company recognized revenue of $313,000 corresponding to the royalties for the six-month period ended June 30, 2003.

3. Other Income

In February 2003, the Company recognized a gain of $376,000 from the sale of the equipment of its pilot plant of Vénissieux.

In March 2003, the Company recognized revenues of $768,000 from conditional grants received from French public agencies. The requirements related to the grants consisted principally in maintaining certain levels of employment, which were achieved in 2003.

4. Inventory

Inventories consist principally of raw materials and finished products, which are stated at the lower of cost (first-in, first-out) or market. The components of inventories were as follows :

(In thousands of U.S. dollars)	June 30, 2003
Raw materials	$ 831
Finished goods	238
Inventories, net	$1,069

5. Shareholders' Equity

Over the 2003 first semester, as a result of exercises of stock options, the Company issued 84,500 ordinary shares, nominal value €0.122 ($0.141) per share.

On the same period, as a result of an exercise of warrants, the Company issued 45,000 ordinary shares, nominal value €0.122 ($0.144) per share.

6. Employee Stock-Option Plans

At June 30, 2003, the Company has options outstanding under various stock option plans, all of which are designed to permit options to be granted that result in no compensation expense under the recognition and measurement principles of APB Opinion No. 25, *Accounting for Stock Issued to Employees*, and related Interpretations (APB 25). In accordance with APB 25, the Company recognizes stock-based employee compensation cost over the vesting period when the options granted under those plans have an exercise price lower than the market value of the underlying common stock on the date of grant. The following table illustrates the effect on net income and earnings per share if the Company had applied the fair value

recognition provisions of FASB Statement No. 123, *Accounting for Stock-based Compensation*, to stock-based employee compensation.

(In thousands of U.S. dollars except share data)	Six Months Ended June 30, 2002	2003
Net income (loss), as reported	$ 959	$(3,324)
Add: Stock-based employee compensation expense included in reported net income (loss), net of related tax effects	10	4
Deduct: Total stock-based employee compensation expense determined under fair value based method for all awards, net of related tax effects	(747)	(687)
Pro forma net income (loss)	$ 222	$(4,007)
Earnings per share:		
Basic, as reported	$0.06	$ (0.20)
Basic, pro forma	0.01	(0.25)
Diluted, as reported	0.06	(0.20)
Diluted, pro forma	0.01	(0.25)

In March 2003, 400,000 options were granted to certain executives, the vesting of which can accelerate upon the achievement of certain targets in 2003. If these targets are not attained, the options will continue to vest over four years in accordance with the terms of the 2003 plan agreement.

7. Subsequent Events

7.1. Shareholders's equity.

At September 19, 2003, the issued and outstanding share capital of the Company consists of 19,291,590 ordinary shares, nominal value of €0.122 per share.

Since June 30, 2003, as a result of exercises of stock options, the Company issued 143,000 ordinary shares, at an average price of €4.746 ($5.30) per share.

In August 2003, as a result of an exercise of warrants, the Company issued 45,000 ordinary shares, at an average price of €4.43 ($4.80) per share.

Since June 2003, the Company issued 2,776,500 ordinary shares at an average price of €3.26 ($3.52) as a result of the exercise of 1,099,000 Class A, 392,500 Class B and 1,285,000 Class C.

7.2. Business update.

On August 27, 2003 the Company announced that it licensed its controlled-release long-acting human insulin product, Basulin, to Brystol-Myers Squibb. The licensing agreement, which is subject to antitrust clearance, provides for an initial payment to the Company of $20 million, additional milestone payments that could reach $145 million and double-digit royalties on the sale of the product once specific sales levels are achieved. Bristol-Myers also has assumed all future development, registration, and marketing costs of the product in exchange for worldwide marketing rights.

PROSPECTUS

October 2, 2003

FLAMEL TECHNOLOGIES S.A.

6,026,500 Ordinary Shares

in the Form of American Depositary Shares

Each American Depositary Share ("ADS") represents one Ordinary Share, approximately 0.122 euro nominal value (the "Shares"), of Flamel Technologies S.A. The ADSs are evidenced by American Depositary Receipts ("ADRs"). See "Description of American Depositary Shares." Our ADSs are listed on the Nasdaq National Market under the symbol "FLML." The closing price on our ADSs on the Nasdaq National Market was $40.20 per ADS on September 23, 2003. We may sell these securities to or through a selected underwriter. We will set forth the name of the selected underwriter in the accompanying prospectus supplement. We will issue up to 2,000,000 new ordinary shares. The selling shareholders named in the accompanying prospectus are selling up to 4,026,500 ADSs.

You should read carefully this prospectus, the documents incorporated by reference in this prospectus and any prospectus supplement before you invest. We strongly recommend that you read carefully the risks we describe in the accompanying prospectus supplement, as well as the risk factors in our most current reports to the Securities and Exchange Commission, for a fuller understanding of the risks and uncertainties that we face. **See "Risk Factors" on page 6.**

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

This prospectus may not be used to consummate sales of securities unless it is accompanied by a prospectus supplement.

The date of this prospectus is October 2, 2003.

TABLE OF CONTENTS

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission ("SEC") using a "shelf" registration process. Under this shelf process, we and the selling shareholders named in the accompanying prospectus supplement may offer, from time to time, in one or more offerings, our Ordinary Shares in the form of ADSs.

We will not offer more than 2,000,000 and the selling shareholders will not offer more than 1,800,000 Ordinary Shares in the form of ADSs under this shelf registration statement. This prospectus provides you with a general description of the securities we or the selling shareholders may offer. Each time we offer securities, we will provide you with a prospectus supplement that will describe the specific amounts, prices and terms of the securities we offer. The prospectus supplement also may add, update or change information contained in this prospectus.

We will sell the securities to or through a selected underwriter. We and our agents reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. The prospectus supplement, which we will provide to you each time we offer securities, will provide the name of the selected underwriter and any applicable fee, commission or discount arrangements with them. The selling stockholders may sell through an underwriter, directly to investors or otherwise. See "Plan of Distribution."

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC under the Securities Act of 1933, as amended (the "Securities Act"), a registration statement on Form F-3. This prospectus does not contain all of the information contained in the registration statement, certain portions of which have been omitted under the rules of the SEC. We also file annual, quarterly and special reports and other information with the SEC under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). The Exchange Act file number for our SEC filings is 000-28508. You may read and copy the registration statement and any other document we file at the following SEC public reference rooms:

Judiciary Plaza 450 Fifth Street, N.W. Rm. 1024 Washington, D.C. 20549	500 West Madison 14th Floor Chicago, Illinois 60661	233 Broadway 13th Floor New York, New York 10279

You may obtain information on the operation of the public reference room in Washington, D.C. by calling the SEC at 1-800-SEC-0330. We file information electronically with the SEC. Our SEC filings are available from the SEC's Internet site at http://www.sec.gov, which contains reports, proxy and information statements and other information regarding issuers that file electronically. You may read and copy our SEC filings and other information at the offices of NASDAQ Operations, 1735 K Street, N.W., Washington, D.C. 20006.

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" the documents we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus. We incorporate by reference the documents listed below:

- our Annual Report on Form 20-F for the fiscal year ended December 31, 2002;
- our Reports of Foreign Private Issuer on Form 6-K pursuant to Rules 13a-16 and 15d-16 filed with the Commission on April 2, May 9, July 15, August 15 and September 17, 2003;
- all documents we subsequently file under Sections 13(a), 13(c) or 15(d) of the Exchange Act after the date of this prospectus and before the termination of the offerings using this prospectus, including

Annual Reports on Form 20-F, provided that with respect to any Report of Foreign Private Issuer on Form 6-K, we will only incorporate these documents to the extent that any report is specifically designated as being incorporated by reference into this prospectus; and

- the description of our Ordinary Shares, nominal value approximately 0.122 euro per share, and the American Depositary Shares representing the Ordinary Shares, contained in our Registration Statement on Form F-1 on April 19, 1996, as amended, pursuant to the Securities Act.

Information that we file with the SEC will automatically update and supercede information in documents filed with the SEC at earlier dates. All information appearing in this prospectus is qualified in its entirety by the information and financial statements, including the notes, contained in the documents that we incorporate by reference into this prospectus.

We will provide a copy of the documents we incorporate by reference, at no cost, to any person who receives this prospectus. To request a copy of any or all of these documents, you should write or telephone us at: Flamel Technologies S.A., 33 Avenue du Docteur Georges Levy, 69693 Vénissieux Cedex, France, (202) 862-8400.

SUMMARY

This summary contains a general summary of the information contained in this prospectus. It may not include all the information that is important to you. You should read the entire prospectus, the prospectus supplement delivered with the prospectus, and the documents incorporated by reference before making an investment decision.

THE COMPANY

Flamel Technologies ("Flamel" or the "Company") is a biopharmaceutical company principally engaged in the development of two unique polymer based delivery systems for medical applications. Our Medusa® nano-encapsulation technology is designed to deliver therapeutic proteins. Our lead product, Basulin®, a long-acting insulin for the treatment of diabetes, is the first application of this patented delivery system. Micropump® is a controlled release technology for the oral administration of small molecules. Asacard™, a controlled-release aspirin, has been approved in the United Kingdom and several other European countries. Genvir™, a second product using Micropump, is a controlled-release acyclovir for the treatment of genital herpes. Our innovative technologies have also been instrumental in the development of a photochromic eyeglass lens product that was launched by Corning in 1999.

Our principal executive offices are located at 33 Avenue du Docteur Georges Levy, 69693 Vénissieux Cedex, France, and our telephone number is (202) 862-8400.

SECURITIES WE ARE OFFERING

American Depositary Shares

We and the selling shareholders may offer American Depositary Shares ("ADS") from time to time. The ADSs are issued under a Deposit Agreement, dated as of June 6, 1996, as amended and restated as of August 10, 2001 (the "Deposit Agreement"), among Flamel, The Bank of New York, as depositary (the "Depositary"), and holders from time to time of ADSs issued thereunder.

Listing

Our ADSs are currently traded on the Nasdaq National Market under the symbol "FLML".

SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus, any prospectus supplement and the documents incorporated herein by reference contain forward-looking statements. Additional written or oral forward-looking statements may be made by the Company from time to time in filings with the SEC or otherwise. The words “believe,” “expect,” “anticipate,” and “project” and similar expressions identify forward-looking statements, which speak only as of the date the statement is made. Such forward-looking statements are within the meaning of that term in Section 27A of the Securities Act and Section 21E of the Exchange Act. Such statements may include, but are not limited to, information regarding revenues, income or loss, capital expenditures, acquisitions, distributions, growth, plans for future operations, financing needs or plans, as well as assumptions relating to the foregoing. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. Future events and actual results could differ materially from those set forth in, contemplated by or underlying the forward-looking statements. Statements in this prospectus, including those set forth in “Risk Factors,” describe factors, among others, that could contribute to or cause such differences.

RISK FACTORS

Investing in our ADSs involves a high degree of risk. Before making an investment decision, you should carefully consider the risk factors set forth in the accompanying prospectus supplement, as well as other information we include or incorporate by reference in this prospectus and the additional information in the other reports we file with the SEC. The risks and uncertainties we have described are not the only ones facing us. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect us.

USE OF PROCEEDS

Unless we specify otherwise in a prospectus supplement, we intend to use the net proceeds from the sales of securities to provide additional funds for our operations and for other general corporate purposes. If net proceeds from a specific offering will be used to repay indebtedness, the applicable prospectus supplement will describe the relevant terms of the debt to be repaid. We will not receive any proceeds from the sale of the ADSs offered by the selling shareholders.

SELLING SHAREHOLDERS

The following table sets forth information with respect to the selling shareholders and the ADSs beneficially owned by each selling shareholder that will be offered under this prospectus supplement.

Name of Beneficial Owner	Number of Ordinary Shares or ADSs Owned Prior to the Offering(1)	Number of ADSs Offered	Number of Ordinary Shares or ADSs Owned After Completion of the Offering
Alta BioPharma Partners, LP(2)	1,351,954	1,351,954	—
Flamel Chase Partners (AltaBio), LLC(2)	772,088	772,088	—
Alta Embarcadero BioPharma Partners, LLC(2)	50,958	50,958	—
Gerard Soula	689,245	300,000	389,245
J.P. Morgan Partners (BHCA), L.P.	101,500	101,500	—
SF Capital(3)	598,426	550,000	48,426
Biotechnology Value Fund, L.P.(4)	945,063	900,000	45,063

(1) Includes options and warrants currently exercisable and exercisable within 60 days.

(2) Alta Partners directly or indirectly provides investment advisory services to various venture capital funds, including Alta BioPharma Partners, L.P. (Alta BioPharma), Alta Embarcadero BioPharma Partners, LLC (Alta Embarcadero) and Flamel Chase Partners (AltaBio), LLC. The general partner of Alta BioPharma, members of Alta Embarcadero and the managing member of Flamel Chase exercise sole voting and investment power with respect to the shares held by the funds.

Certain principals of Alta Partners are managing directors of Alta BioPharma Management Partners, LLC, Alta/Chase Management Partners LLC (the General Partner of Alta BioPharma and the Managing Member of Flamel Chase), and members of Alta Embarcadero. As managing directors and members, they may be deemed to share voting and investment powers of the shares held by the funds. These principals disclaim beneficial ownership of all such shares held by the aforementioned funds, except to the extent of their proportionate pecuniary interests therein.

(3) Sole voting and dispositive power over the shares beneficially owned by SF Capital is held by Michael A. Roth and Brian J. Stark in their capacity as managing members of Staro Asset Management, LLC, the investment manager of SF Capital.

(4) Includes shares held by Biotechnology Value Fund, L.P. and its affiliates, Biotechnology Value Fund II, L.P., Investment 10, L.L.C., BVF Partners L.P. and BVF Inc.

PLAN OF DISTRIBUTION

We and the selling shareholders may sell in the United States the securities being offered hereby from time to time to a selected underwriter for resale to the public or directly to investors.

We will set forth in a prospectus supplement the terms of the offering of the securities, including:

- the name of the selected underwriter;
- the purchase price of the securities being offered and approximate amount of the proceeds we will receive from the sale;
- any agency fees or underwriting discounts and other items constituting the underwriter's compensation;
- any initial public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchanges on which the Ordinary Shares in the form of ADSs may be listed.

The selling shareholders and their successors, including its transferees, pledgees or donees or their successors, may sell ADSs directly to purchasers or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions from the selling shareholders or the purchasers. These discounts, concessions or commissions as to any particular underwriter, broker-dealer or agent may be in excess of those customary in the types of transactions involved.

The selling shareholders' ADSs may be sold in one or more transactions at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market prices, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions:

- on any national securities exchange or U.S. inter-dealer system of a registered national securities association on which the ADSs may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in transactions otherwise than on these exchanges or systems or in the over-the-counter market;
- through the writing of options, whether the options are listed on an options exchange or otherwise; or
- through the settlement of short sales.

In connection with the sale of the ADSs, the selling shareholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the ADSs in the course of hedging the positions they assume. The selling shareholders may also sell the ADSs short and deliver these securities to close out their short positions, or loan or pledge ADSs to broker-dealers that in turn may sell these securities.

The aggregate proceeds to the selling shareholders from the sale of the ADSs will be the purchase price of the ADSs less discounts and commissions, if any. The selling shareholders reserve the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of ADSs to be made directly or through agents. We will not receive any of the proceeds from the offering made by the selling shareholders.

Agents

We may designate agents who agree to use their reasonable or best efforts to solicit purchases for the period of their appointment or to sell securities on a continuing basis.

Underwriter

The selected underwriter will acquire the securities for its own account. The selected underwriter may resell the securities in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the selected underwriter to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. The underwriter will be obligated to purchase all the securities of the series offered if it purchases any of the securities of that series. We may change from time to time any initial public offering price and any discounts or concessions the underwriters allow or reallow or pay to dealers. We may use an underwriter with whom we have a material relationship. We will describe in the prospectus supplement naming the selected underwriter the nature of any such relationship.

Trading Markets And Listing Of American Depositary Shares

Our ADSs are listed on the Nasdaq National Market. We may elect to list any other class or series of securities on any exchange, but we are not obligated to do so. It is possible that one or more underwriters may make a market in a class or series of securities, but the underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot give any assurance as to the liquidity of the trading market for any of the securities.

Stabilization Activities

Any underwriter may engage in stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Passive Market Making

Any underwriters who are qualified market makers on the NASDAQ Stock Market may engage in passive market making transactions in the securities on the NASDAQ Stock Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker’s bid, however, the passive market maker’s bid must then be lowered when certain purchase limits are exceeded.

DESCRIPTION OF SHARE CAPITAL

Set forth below is certain information concerning Flamel’s share capital together with related summary information concerning certain provisions of Flamel’s *statuts* and applicable French law. Such description of Flamel’s share capital and summary information are qualified in their entirety by reference to Flamel’s *statuts* which has been filed as an exhibit to Flamel’s Registration Statement on Form F-1 filed on April 19, 1996, as amended.

General

The share capital of Flamel consists of ordinary shares, nominal value approximately 0.122 euro per share. As of August 18, 2003, the issued and outstanding share capital of the Company was 16,884,090

ordinary shares. All of the shares, including the shares to be sold in this offering, are or will be fully paid. Pursuant to Flamel's *statuts*, the shares may be held only in registered form on the books and records of the Company. See "— Form and Holding of Shares."

Changes in Share Capital

Except as set forth below, the share capital of Flamel may be increased only with the approval of the shareholders at an extraordinary general meeting, following a recommendation of the Board of Directors. Increases in share capital may be effected either by the issuance of additional shares, by an increase in the nominal value of existing shares or by the creation of a new class of shares. Additional shares may be issued for cash, in satisfaction of indebtedness incurred by Flamel or for assets contributed in kind, upon the conversion, exchange or redemption of debt securities previously issued by Flamel, upon the exercise of stock options, warrants or other similar securities comprising rights to subscribe for shares, or by capitalization of reserves. Share dividends may be distributed in lieu of payment of cash dividends, as described under "— Dividend and Liquidation Rights."

French law requires that the net assets of a corporation as calculated under French statutory accounting be equal to at least one-half of its issued nominal capital (*capital social*). The board of directors of any such French corporation must, within four months from the approval by the shareholders of the audited accounts showing such a deficiency in the net asset position, convene an extraordinary meeting of shareholders in order to decide whether the corporation ought to be dissolved before its statutory term or whether to continue the business activity of the corporation. If the dissolution is not declared, the net asset position must then be restored at the latest at the end of the second fiscal year following the fiscal year during which the insufficient net asset position was legally established by the shareholders.

The shareholders of Flamel have authorized the Board of Directors of Flamel to the increase the share capital related to the securities being offered by the Company in this offering in one or several issuances, up to an amount of 2,000,000 new shares. The shareholders of Flamel have also decided that the final share purchase price shall be a minimum of $12 per share and no less than 90% of the market price for the shares on the trading day immediately preceding the subscription of the shares and that the share purchase price for each issued share, to be set by the Board of Directors, will thus depend on the Company's stock price on the day preceding the transaction in order to be compliant with the conditions mentioned above, under the supervision of Flamel's statutory auditor. Unless repealed by the shareholders, this authorization will be in effect for a period that will expire at the end of the shareholders' meeting of Flamel called on to rule on the financial statements for the fiscal year ending December 31, 2003.

The shares issued or which may be issued upon exercise of warrants and stock options authorized pursuant to our shareholder resolutions approving our capital increases at extraordinary general shareholders' meetings held between July 19, 2001 and February 18, 2003 may be voided because our shareholders were not asked to vote on resolutions which would reserve a capital increase for the sole benefit of our employees as required by French law. We intend to convene an extraordinary general meeting of shareholders as soon as practicable to ratify the votes taken at these shareholder meetings.

Additionally, the issuance of certain shares in 1990 and 1996 may have been voidable under French law. However, the statute of limitations with respect to those share issuances has expired, and the validity of those shares may no longer be challenged.

Warrants and Options

As of September 17, 2003, the Company has outstanding two series of warrants held by investors. The first such series consists of 700,000 warrants exercisable at a price of €5.96 per share at any time prior to March 23, 2005. The second such series consists of 250,000 warrants exercisable at a price of €5.96 per share at any time prior to March 23, 2005. These warrants are not evidenced by any separate certificates but rather are registered in the names of the respective holders on the books and records of the Company.

On June 13, 2003, the Company's Board of Directors proposed issuing warrants to certain directors to purchase 200,000 ordinary shares at an exercise price of €9.88 and expects to submit this proposal for approval by its shareholders at the next extraordinary meeting of shareholders. The Company expects to

record a compensation charge as the options vest in an amount equal to the difference in value between the exercise price and the Company's stock price on the date of shareholder approval.

In March 2003, 400,000 options were granted to certain executives the vesting of which can accelerate upon the achievement of certain targets in 2003. If these targets are not attained, the options will continue to vest over four years in accordance with the terms of the 2003 plan agreement.

Preemptive Subscription Rights

Unless previously waived or cancelled, holders of shares have preemptive rights to subscribe for additional shares issued by Flamel for cash on a pro rata basis. Shareholders may individually waive such preemptive subscription rights or cancel all of them at an extraordinary general meeting under certain circumstances. Preemptive subscription rights, if not previously cancelled by an extraordinary general meeting or individually waived by each shareholder, are transferable during the subscription period relating to a particular offering of shares, unless otherwise decided by the extraordinary general meeting. Flamel's shareholders' meeting has cancelled the shareholders' preemptive rights with respect to the issuance of the shares by the Company to or through the selected underwriter in connection with this offering.

Attendance and Voting at Shareholders' Meetings

In accordance with French law, there are two types of shareholders' general meetings, ordinary and extraordinary. Ordinary general meetings of shareholders are required for matters such as the election of directors, the appointment of statutory auditors, the approval of the annual report prepared by the Board of Directors and the annual accounts, the declaration of dividends and the issuance of bonds.

Extraordinary general meetings of shareholders are required for approval of matters such as amendments to Flamel's *statuts*, modification of shareholders' rights, approval of mergers, increases or decreases in share capital, the creation of a new class of capital stock and the authorization of the issuance of investment certificates or securities convertible or exchangeable into shares. In particular, shareholder approval will be required for any and all mergers in which (i) the Company is not the surviving entity or (ii) the Company is the surviving entity but in connection with which the Company is issuing a portion of its share capital to the acquired entity.

The Board of Directors is required to convene an annual ordinary general meeting of shareholders, which must be held within six months of the end of Flamel's fiscal year, which is December 31. Other ordinary or extraordinary meetings may be convened at any time during the year. Meetings of shareholders may be convened by the Board of Directors or, if the Board of Directors fails to call such a meeting, by Flamel's designated statutory auditors, currently Ernst & Young Audit, or by an agent appointed by the court. The court may be requested to appoint such an agent either by shareholder(s) holding at least 5% of Flamel's share capital or by an interested party or the works council in cases of urgency. Following a successful take-over bid or the acquisition of control of the Company, the new majority shareholders may call a shareholders' ordinary or extraordinary general meeting, depending on matters to be considered in such meeting. The notice calling such meeting must state the matters to be considered.

French law provides that, at least 15 days before the date set for any general meeting on first notice, and at least six days before the date set for any general meeting on second notice, notice of the meeting must be sent by mail to all holders of properly registered shares who have held such shares prior to the date of the notice. A preliminary written notice (*avis de reunion*) must be sent to each shareholder who has requested to be notified in writing before the date set for any ordinary or extraordinary general meeting. Shareholders holding a defined percentage of the share capital of the Company, which varies depending on the absolute amount of the share capital, may propose resolutions to be submitted for approval by the shareholders at the meeting. The defined percentage referred to in the preceding sentence will never be higher than five percent. Holders of ADSs will receive notice of shareholders' meetings and other reports and communications that are made generally available to shareholders from the Depositary if we furnish sufficient copies of the documents and ask the Depositary to mail them to ADR holders. See "Description of American Depositary Shares —

Voting of the Underlying Shares" for the contents and time periods for notices of shareholder meetings to be given to the holders of ADSs.

Attendance and exercise of voting rights at ordinary general meetings and extraordinary general meetings of shareholders are subject to certain conditions. Pursuant to the Company's *statuts*, holders of shares deciding to exercise their voting rights must have their Shares registered in their names in the shareholder registry maintained by or on behalf of Flamel one day prior to the meeting at the latest. Certain procedures to effect such requirements will apply to a holder of ADSs desiring to exercise the voting rights relating to the shares corresponding to such ADSs. See "Description of American Depository Shares — Voting of the Underlying Shares."

All shareholders who have properly registered their shares have the right to participate in general meetings, either in person, by proxy or by mail, and to vote according to the number of shares they hold. Each share confers on the shareholder the right to one vote. Under French law, shares held by entities controlled directly or indirectly by Flamel shall not be entitled to any voting rights. A proxy may be granted by a shareholder whose name is reflected on the Company's share registry to his or her spouse, to another shareholder or to a legal representative, in the case of a legal entity, or by sending a proxy in blank to the Company without nominating any representative. In the latter case, the chairman of the meeting of shareholders will vote the Shares with respect to which such blank proxy has been given in favor of all resolutions proposed by the Board of Directors and against all others.

The presence in person or by proxy of shareholders holding not less than 25% (in the case of an ordinary meeting) or 33.3% (in the case of an extraordinary meeting) of the shares entitled to vote is necessary for a quorum. If a quorum is not present at an initial meeting, then the meeting must be adjourned. An adjourned meeting may be reconvened upon six days' notice. Upon recommencement of an adjourned meeting, no quorum is required in the case of an ordinary general meeting but, in the case of an extraordinary meeting, the presence in person or by proxy of shareholders holding not less than 25% of the shares entitled to vote is required for a quorum.

At an ordinary meeting, a simple majority of the votes cast is required to pass a resolution. At an extraordinary general meeting, a two-thirds majority of the votes cast is required. However, a unanimous vote is required to increase liabilities of shareholders. Abstention by those present or represented by proxy is deemed a vote against the resolution submitted to a vote.

In addition to rights to certain information regarding Flamel, any shareholder may, during the 15 day period preceding a shareholders' meeting, submit written questions to the Board of Directors relating to the agenda for the meeting. The Board of Directors is required to respond to such questions during the meeting.

As set forth in the *statuts*, shareholders' meetings are held at the registered office of the Company or at any other location specified in the written notice.

Dividend and Liquidation Rights

As provided under French law, net income in each fiscal year (after deduction for legal reserve), as increased or reduced, as the case may be, by any net income or loss of any French corporation carried forward from prior years, is available for distribution to the shareholders of such corporation as dividends, all as determined in accordance with French statutory accounting. Dividends may also be distributed from available reserves of any French corporation, subject to approval by the shareholders and certain limitations.

Under French law, a corporation is legally required to establish and maintain a legal reserve by making a minimum transfer of 5% of its net income in each year to such legal reserve as may be necessary to maintain it at a level equal to 10% of the aggregate nominal value of its share capital, as increased or reduced from time to time. The legal reserve is distributable only upon liquidation. The payment of dividends, if any, is fixed by the ordinary general meeting of shareholders at which the annual accounts are approved following recommendation of the Board of Directors. Dividends are payable pro rata to holders of shares outstanding on the date of the shareholder meeting approving the distribution of dividends or, in the case of interim dividends, on the date of the meeting of the Board of Directors approving the distribution of interim

dividends. The actual dividend payment date is determined by the shareholders at the ordinary general meeting approving the declaration of the dividends or by the Board of Directors in the absence of such determination by the shareholders. The payment of the dividends must occur within nine months of the end of a French company's fiscal year. Dividends not claimed within five years of the date of payment revert to the French state. The *statuts* of the Company authorize the shareholders, in an ordinary general meeting, to authorize the grant to each shareholder of an option to receive all or part of any annual or interim dividends either in cash or shares.

If net income (as shown on an interim income statement certified by Flamel's statutory auditors) is sufficient, the Board of Directors has the authority, subject to French law and regulations, without the approval of shareholders, to distribute interim dividends.

In the event that Flamel is liquidated, the assets of Flamel remaining after payment of its debts, liquidation expenses and all of its remaining obligations will be distributed first to repay in full the capital of the shares, and the surplus, if any, will then be distributed pro rata among the holders of shares in proportion to the nominal value of their shareholdings and subject to any special rights granted to holders of priority shares, if any.

Repurchase of Shares

Pursuant to French law, Flamel may not acquire its shares except in certain limited circumstances not presently applicable to it.

Form and Holding of Shares

Form of Shares. Flamel's *statuts* provides that shares may be held only in registered form.

Holding of Shares. Shares are registered in the name of the respective owners thereof in the registry maintained by or on behalf of Flamel. Stock certificates evidencing shares, in a manner comparable to that in the United States, are not issued by French companies, but the Company may issue or cause to be issued confirmations as to holdings of shares registered in such registry to the persons in whose name such shares are registered. Such confirmations do not constitute documents of title and are not negotiable instruments.

DESCRIPTION OF AMERICAN DEPOSITARY RECEIPTS

The following is a summary of the material provisions of the Deposit Agreement. This summary is qualified in its entirety by reference to the Deposit Agreement, which has been filed as an exhibit to Post-Effective Amendment No. 1 to Flamel's Registration Statement on Form F-6 filed on July 26, 2001, as amended. Additional copies of the Deposit Agreement are available for inspection at the Corporate Trust Office of the Depositary in New York, which is presently located at 101 Barclay Street, New York, New York 10286. As used herein, the term "ADR holder" shall mean a person in whose name an American Depositary Receipt ("ADR") is registered on the books of the Depositary maintained for such purpose. Capitalized terms not defined herein shall have the respective meanings assigned to them by the Deposit Agreement.

American Depositary Receipts

The Depositary will execute and deliver the ADRs. Each ADR is a certificate evidencing a specific number of ADSs. Each ADS represents one Ordinary Share (or a right to receive one Ordinary Share) deposited with the Depositary or the Paris office of Credit Lyonnais, as custodian (the "Custodian"), for the Depositary presently located at 19 Boulevard des Italiens, 75002 Paris, France. Each ADS will also represent any other securities, cash or other property that may be held by the Depositary.

You may hold ADSs either directly (by having an ADR registered in your name) or indirectly through your broker or other financial institution. If you hold ADSs directly, you are an ADR holder. This description assumes you hold your ADSs directly. If you hold the ADSs indirectly, you must rely on the procedures of

your broker or other financial institution to assert the rights of ADR holders described in this section. You should consult with your broker or financial institution to find out what those procedures are.

As an ADR holder, we will not treat you as one of our shareholders and you will not have shareholder rights. French law governs shareholder rights. The Depositary will be the holder of the Ordinary Shares underlying your ADSs. As a holder of ADRs, you will have ADR holder rights. The Deposit Agreement sets forth ADR holder rights as well as the rights and obligations of the Depositary. New York law governs the Deposit Agreement and the ADRs.

Dividends and Other Distributions

The Depositary has agreed to pay to you the cash dividends or other distributions it or the Custodian receives on the Ordinary Shares or other deposited securities, after deducting its fees and expenses. You will receive these distributions in proportion to the number of shares your ADSs represent.

- ***Cash.*** The Depositary will convert any cash dividend or other cash distribution we pay on the shares into U.S. dollars, if it can do so on a reasonable basis and can transfer the U.S. dollars to the United States. If that is not possible or if any government approval is needed and cannot be obtained, the Deposit Agreement allows the Depositary to distribute the foreign currency only to those ADR holders to whom it is possible to do so. It will hold the foreign currency it cannot convert for the account of the ADR holders who have not been paid. It will not invest the foreign currency and it will not be liable for any interest.

  Before making a distribution, the Depositary will deduct any withholding taxes that must be paid. It will distribute only whole U.S. dollars and cents and will round fractional cents to the nearest whole cent. *If the exchange rates fluctuate during a time when the Depositary cannot convert the foreign currency, you may lose some or all of the value of the distribution.*

- ***Shares.*** The Depositary may distribute additional ADRs representing any shares we distribute as a dividend or free distribution. The Depositary will only distribute whole ADRs. It will sell shares that would require it to deliver a fractional ADRs and distribute the net proceeds in the same way as it does with cash. If the Depositary does not distribute additional ADRs, the outstanding ADRs will also represent the new shares.

- ***Rights to purchase additional shares.*** If we offer holders of our securities any rights to subscribe for additional shares or any other rights, the Depositary may make these rights available to you. If the Depositary decides it is not legal and feasible to make the rights available but that it is feasible to sell the rights, the Depositary will use reasonable efforts to sell the rights and distribute the proceeds in the same way as it does with cash. The Depositary will allow rights that are not distributed or sold to lapse. *In that case, you will receive no value for them.*

  If the Depositary makes rights available to you, it will exercise the rights and purchase the shares on your behalf. The Depositary will then deposit the shares and deliver ADRs to you. It will only exercise rights if you pay it the exercise price and any other charges the rights require you to pay.

  U.S. securities laws may restrict transfers and cancellation of the ADRs represented by shares purchased upon exercise of rights. For example, you may not be able to trade these ADRs freely in the United States. In this case, the Depositary may deliver restricted ADRs that have the same terms as the ADRs described in this section except for changes needed to put the necessary restrictions in place.

- ***Other Distributions.*** The Depositary will send to you anything else we distribute on deposited securities by any means it thinks is legal, fair and practical. If it cannot make the distribution in that way, the Depositary has a choice. It may decide to sell what we distributed and distribute the net proceeds, in the same way as it does with cash. Or it may decide to hold what we distributed, in which case ADSs will also represent the newly distributed property. However, the Depositary is not

required to distribute any securities (other than ADSs) to you unless it receives satisfactory evidence from us that it is legal to make that distribution.

The Depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any ADR holder. We have no obligation to register ADSs, shares, rights or other securities under the Securities Act. We also have no obligation to take any other action to permit the distribution of ADRs, ADSs, shares, rights or anything else to ADR holders. *This means that you may not receive the distributions we make on our shares or any value for them if it is illegal or impractical for us to make them available to you.*

Deposit, Withdrawal and Cancellation

The Depositary will deliver ADRs if you or your broker deposits shares or evidence of rights to receive shares with the Custodian or the Depository. Upon payment of its fees and expenses and of any taxes or charges, such as stamp taxes or stock transfer taxes or fees, the Depositary will register the appropriate number of ADSs in the names you request and will deliver the ADRs at its office to the persons you request.

You may turn in your ADRs at the Depositary's office. Upon payment of its fees and expenses and of any taxes or charges, such as stamp taxes or stock transfer taxes or fees, the Depositary will transfer the shares and any other deposited securities underlying the ADR to you or a person you designate at the office of the Custodian. Or, at your request, risk and expense, the Depositary will deliver the deposited securities at its office, if feasible.

Voting of the Underlying Shares

You may instruct the Depositary to vote the Ordinary Shares underlying your ADRs, but only if we ask the Depositary to ask for your instructions. *Otherwise, you will not be able to exercise your right to vote unless you withdraw the shares. However, you may not know about the meeting enough in advance to withdraw the shares.*

If we ask for your instructions, the Depositary will notify you of the upcoming vote and arrange to deliver our voting materials to you. The materials will (1) describe the matters to be voted on and (2) explain how you may instruct the Depositary to vote the Ordinary Shares or other deposited securities underlying your ADSs as you direct. For instructions to be valid, the Depositary must receive them on or before the date specified. The Depositary will try, as far as practical, subject to French law and the provisions of our *statuts*, to vote or to have its agents vote the shares or other deposited securities as you instruct.

If the Depositary does not receive voting instructions from you by the specified date, it will consider you to have authorized and directed it to vote the number of deposited securities represented by your ADSs in accordance with the recommendations of our management. *However*, the Depositary will not vote under the preceding sentence if we notify the Depositary that:

- we do not wish it to do so;
- we think there is substantial shareholder opposition to the particular question; or
- we think the particular question would have an adverse impact on our shareholders.

The Depositary will only vote or attempt to vote as you instruct or as described in this paragraph.

We cannot assure you that you will receive the voting materials on time to ensure that you can instruct the Depositary to vote your Ordinary Shares. In addition, the Depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. *This means that you may not be able to exercise your right to vote and there may be nothing you can do if your shares are not voted as you requested.*

Fees and Expenses

Persons depositing shares: or ADR holders must pay:	For:
1. $5.00 (or less) per 100 ADSs (or portion of 100 ADSs)	• Execution and delivery of ADRs, including issuances resulting from a distribution of shares or rights or other property • Cancellation of ADRs for the purpose of withdrawal, including if the Deposit Agreement terminates
2. $.02 (or less) per ADS	• Any cash distribution to you
3. A fee equivalent to the fee that would be payable if securities distributed to you had been shares and the shares had been deposited for issuance of ADSs	• Distribution of securities distributed to holders of deposited securities which are distributed by the Depositary to ADR holders
4. $1.50 or less per certificate	• Registration of transfer of ADRs
5. Registration or transfer fees	• Transfer and registration of shares on our share register to or from the name of the Depositary or its agent when you deposit or withdraw shares
6. Expenses of the Depositary	• Cable, telex and facsimile transmissions (when expressly provided in the Deposit Agreement)
7. Taxes and other governmental charges the Depositary or the custodian has to pay on any ADR or share underlying an ADR, for example, stock transfer taxes, stamp duty or withholding taxes	
8. Expenses of the Depositary in converting foreign currency to U.S. dollars	

Payment of Taxes

The Depositary may deduct the amount of any taxes owed from any payments to you. It may also sell deposited securities, by public or private sale, to pay any taxes owed. You will remain liable if the proceeds of the sale are not enough to pay the taxes. If the Depositary sells deposited securities, it will, if appropriate, reduce the number of ADSs to reflect the sale and pay to you any proceeds, or send to you any property, remaining after it has paid the taxes.

Reclassifications, Recapitalizations and Mergers

If we (i) change the nominal value of our shares, (ii) reclassify, split up or consolidate any of the deposited securities, (iii) distribute securities on the shares that are not distributed to you or (iv) recapitalize, reorganize, merge, liquidate, sell all or substantially all of our assets, or take any similar action, then:

- the cash, shares or other securities received by the Depositary will become deposited securities. Each ADS will automatically represent its equal share of the new deposited securities; and

- the Depositary may, and will if we ask it to, distribute some or all of the cash, shares or other securities it received. It may also deliver new ADRs or ask you to surrender your outstanding ADRs in exchange for new ADRs identifying the new deposited securities.

Amendment and Termination

We may agree with the Depositary to amend the Deposit Agreement and the ADRs without your consent for any reason. If an amendment adds or increases fees or charges, except for taxes and other governmental

charges or expenses of the Depositary for registration fees, facsimile costs, delivery charges or similar items, or prejudices a substantial right of ADR holders, it will not become effective for outstanding ADRs until 60 days after the Depositary notifies ADR holders of the amendment. *At the time an amendment becomes effective, you are considered, by continuing to hold your ADR, to agree to the amendment and to be bound by the ADRs and the Deposit Agreement as amended.*

The Depositary will terminate the Deposit Agreement if we ask it to do so. The Depositary may also terminate the Deposit Agreement if the Depositary has told us that it would like to resign and we have not appointed a successor Depositary within 90 days. In either case, the Depositary must notify you at least 90 days before termination.

After termination, the Depositary and its agents will do the following under the Deposit Agreement but nothing else: (1) advise you that the Deposit Agreement is terminated, (2) collect distributions on the deposited securities, (3) sell rights and other property and (4) deliver shares and other deposited securities upon cancellation of ADRs. One year after termination, the Depositary may sell any remaining deposited securities by public or private sale. After that, the Depositary will hold the money it received on the sale, as well as any other cash it is holding under the Deposit Agreement, for the pro rata benefit of the ADR holders that have not surrendered their ADRs. It will not invest the money and has no liability for interest. The Depositary's only obligations will be to account for the money and other cash. After termination, our only obligations will be to indemnify the Depositary and to pay fees and expenses of the Depositary that we have agreed to pay.

Limitations on Obligations and Liability

The Deposit Agreement expressly limits our obligations and the obligations of the Depositary. It also limits our liability and the liability of the Depositary. The Depositary and we:

- are only obligated to take the actions specifically set forth in the Deposit Agreement without negligence or bad faith;
- are not liable if either of us is prevented or delayed by law or circumstances beyond our control from performing our obligations under the Deposit Agreement;
- are not liable if either of us exercises discretion permitted under the Deposit Agreement;
- have no obligation to become involved in a lawsuit or other proceeding related to the ADRs or the Deposit Agreement on your behalf or on behalf of any other party; and
- may rely upon any documents we believe in good faith to be genuine and to have been signed or presented by the proper party.

In the Deposit Agreement, we agree to indemnify the Depositary for acting as Depositary, except for losses caused by the Depositary's own negligence or bad faith.

Requirements for Depositary Actions

Before the Depositary will deliver or register a transfer of an ADR, make a distribution on an ADR, or permit withdrawal of shares, the Depositary may require:

- payment of stock transfer or other taxes or other governmental charges and transfer or registration fees charged by third parties for the transfer of any shares or other deposited securities;
- satisfactory proof of the identity and genuineness of any signature or other information it deems necessary; and
- compliance with regulations it may establish, from time to time, consistent with the Deposit Agreement, including presentation of transfer documents.

The Depositary may refuse to deliver ADRs or register transfers of ADRs generally when the transfer books of the Depositary or our transfer books are closed or at any time if the Depositary or we think it advisable to do so.

Your Right to Receive the Shares Underlying your ADRs

You have the right to cancel your ADRs and withdraw the underlying shares at any time except:

- when temporary delays arise because (i) the Depositary has closed its transfer books or we have closed our transfer books, (ii) the transfer of shares is blocked to permit voting at a shareholders' meeting or (iii) we are paying a dividend on our shares;

- when you or other ADR holders seeking to withdraw shares owe money to pay fees, taxes and similar charges; and

- when it is necessary to prohibit withdrawals in order to comply with any laws or governmental regulations that apply to ADRs or to the withdrawal of shares or other deposited securities.

This right of withdrawal may not be limited by any other provision of the Deposit Agreement.

Pre-release of ADRs

The Deposit Agreement permits the Depositary to deliver ADRs before deposit of the underlying shares. This is called a pre-release of ADRs. The Depositary may also deliver shares upon cancellation of prereleased ADRs (even if the ADRs are canceled before the pre-release transaction has been closed out). A prerelease is closed out as soon as the underlying shares are delivered to the Depositary. The Depositary may receive ADRs instead of shares to close out a pre-release. The Depositary may pre-release ADRs only under the following conditions: (1) before or at the time of the pre-release, the person to whom the pre-release is being made represents to the Depositary in writing that it or its customer owns the shares or ADRs to be deposited; (2) the pre-release is fully collateralized with cash or other collateral that the Depositary considers appropriate; and (3) the Depositary must be able to close out the pre-release on not more than five business days' notice. In addition, the Depositary will limit the number of ADSs that may be outstanding at any time as a result of pre-release to thirty percent (30%) of the Ordinary Shares deposited, although the Depositary may disregard the limit from time to time, if it thinks it is appropriate to do so.

LEGAL MATTERS

Cariddi, Mee, Rué / Hogan & Hartson L.L.P., Paris, France, will provide us with an opinion as to French legal matters and Hogan & Hartson L.L.P., Baltimore, Maryland will provide us with an opinion as to United States legal matters in connection with the securities we are offering.

EXPERTS

The consolidated financial statements of Flamel Technologies S.A. at December 31, 2002 and 2001, and for each of the three years in the period ended December 31, 2002, included in the Prospectus Supplement of Flamel Technologies S.A., which is referred to and made a part of this Prospectus and Registration Statement, have been audited by Ernst & Young Audit, independent auditors, as set forth in their report included therein. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given authority of such firm as experts in accounting and auditing.

3,988,500 Ordinary Shares

FLAMEL TECHNOLOGIES S.A.

Ordinary Shares in the Form of American Depositary Shares

PROSPECTUS SUPPLEMENT

Merrill Lynch & Co.

UBS Investment Bank
SG Cowen
Punk, Ziegel & Company
Merriman Curhan Ford & Co.
Brean Murray & Co., Inc.

October 2, 2003