ESPERION THERAPEUTICS INC/MI
Form 424A
July 18, 2003

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The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it secure an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Filed pursuant to Rule 424(a) under the Securities Act of 1933
Registration No. 333-106988

Subject to Completion, dated July 18, 2003

PROSPECTUS

4,000,000 Shares

Common Stock

We are offering 4,000,000 shares of our common stock, par value $0.001 per share.

Our common stock is quoted on The Nasdaq National Market under the symbol ESPR. On July 16, 2003, the last reported sale price of our common stock was $19.99 per share.

Investing in our common stock involves risks. Risk Factors begin on page 6.

	Per Share	Total
Public offering price	$	$
Underwriting discount and commission	$	$
Proceeds to Esperion Therapeutics, Inc. (before expenses)	$	$

We and certain selling stockholders have granted the underwriters a 30-day option to purchase up to an additional 600,000 shares of our common stock, on the same terms as set forth above, to cover over-allotments.

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.

Lehman Brothers, on behalf of the underwriters, expects to deliver the shares on or about , 2003.

LEHMAN BROTHERS

CITIGROUP

NEEDHAM & COMPANY, INC.

U.S. BANCORP PIPER JAFFRAY

SG COWEN

, 2003

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. You should read the following summary together with the more detailed information regarding our company, our common stock and the financial statements and notes to those statements incorporated herein by reference from our other filings with the Securities and Exchange Commission (the SEC). We urge you to read the entire prospectus carefully, especially the risks of investing in our common stock, which are discussed under Risk Factors, before making an investment decision.

Esperion Therapeutics, Inc.

Esperion Therapeutics, Inc. is a biopharmaceutical company dedicated to the discovery, development and commercialization of therapies to improve the treatment of cardiovascular disease. Our initial focus is on the development and commercialization of novel classes of drugs that focus on a new treatment approach based upon our understanding of high density lipoprotein, or HDL, function. We call this approach HDL Therapy. By exploiting the beneficial properties of HDL, or good cholesterol, to remove excess cholesterol and other lipids from artery walls and other tissues, we believe our portfolio of product candidates offers an innovative approach in the fight against cardiovascular disease. While current therapies are designed to slow the progression of cardiovascular disease, we believe HDL Therapy has the potential to reverse the damaging effects of cholesterol deposits within artery walls.

We currently have four product candidates in clinical development, including three biopharmaceuticals: ETC-588, or LUV; ETC-216, or AIM; and ETC-642, or RLT Peptide; and one oral small molecule, ETC-1001, each targeted at cardiovascular disease or its risk factors. Our biopharmaceuticals are being developed to focus on the acute treatment of high-risk atherosclerosis, such as acute coronary syndromes, while our oral small molecule targets chronic treatment of risk factors associated with cardiovascular disease.

We are also pursuing the discovery and development of orally active organic small molecules designed to increase HDL-cholesterol, or HDL-C, levels and enhance the function of HDL and to decrease low density lipoprotein-cholesterol, LDL-C, or bad cholesterol, levels and triglycerides, another type of lipid, or fat. We believe some of these oral small molecules may possess anti-diabetic and anti-obesity properties.

We believe our product candidates will enhance the naturally occurring processes in the body for the removal of excess cholesterol and other lipids from artery walls and other tissues by enhancing the efficiency of the reverse lipid transport, or RLT, pathway. The RLT pathway is a four-step process through which excess cholesterol and other lipids are removed from artery walls and other tissues. We believe this removal of excess cholesterol and other lipids from artery walls and other tissues will lead to improvements in vascular structure by stabilizing vulnerable plaque, which could ultimately lead to a reduction in clinical events resulting from cardiovascular disease, including atherosclerosis.

Results of clinical trials and pre-clinical studies indicate that ETC-588, ETC-216 and ETC-642 demonstrate mobilization of cholesterol, which is the removal of excess cholesterol from artery walls and other tissues, as evidenced by measurements of the amount of cholesterol and other lipids in the blood before and after administration. The current clinical development status of our product candidates is as follows:

ETC-588 (Phase II): Enrollment in one of our two ongoing Phase II studies was completed in July 2003. The objective of this study is to evaluate the safety and tolerability of ETC-588 in approximately 150 patients with acute coronary syndromes. We continue to enroll patients in another Phase II clinical trial for ETC-588, which was initiated in 2002. This Phase II trial uses magnetic resonance imaging (MRI) technology to examine the effect, if any, of ETC-588 on plaque in the carotid arteries and whether the benefits of therapy persist three months after completion of treatment.

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ETC-216 (Phase II): In June 2003, we reported initial results that showed that our multiple-dose, multi-center Phase II clinical study met its primary efficacy objective of demonstrating statistically significant regression of atherosclerosis with ETC-216. The results of this study demonstrated, for the first time in a clinical trial, statistically significant regression of atherosclerosis at the end of six weeks.

ETC-642 (Phase I): In June 2003, we initiated our first multiple-dose, multi-center clinical trial in up to 32 patients with stable cardiovascular disease. The primary objective of this study is to assess potential dosing levels and regimens for ETC-642 while evaluating safety and tolerability. In 2002, a Phase I single escalating dose clinical trial for ETC-642 was initiated in patients with stable cardiovascular disease and is continuing to enroll patients in order to determine the maximum tolerated dose.

ETC-1001 (Phase I): We recently initiated our first clinical trial for ETC-1001 in healthy volunteers. This trial is a double-blind, placebo-controlled trial designed to evaluate the safety and tolerability of single escalating doses of ETC-1001.

We believe our drug discovery technology and scientific and drug development expertise have potential applicability to the discovery and development of therapies for a broad range of vascular diseases, including treatments for coronary heart disease, peripheral arterial disease (atherosclerosis occurring in arteries near the body s extremities) and stroke.

Our Strategy

Our objective is to discover, develop and commercialize therapies to address significant unmet needs associated with cardiovascular disease by exploiting the beneficial properties of HDL. The key elements of our business strategy are as follows:

discover novel cardiovascular product candidates that overcome limitations of existing treatments;

develop and commercialize a portfolio of drug candidates focused on enhancing the RLT pathway, utilizing the beneficial properties of HDL;

leverage the scientific, drug discovery and drug development expertise and experience of our management team;

enter into strategic collaborations with established pharmaceutical companies in which we retain co-development and co-promotion rights to our biopharmaceutical product candidates; and

focus on the development of biopharmaceutical product candidates for acute treatments and orally active small molecules for chronic therapies to complement statins and other lipid regulating treatments.

Recent Developments

In June 2003, we announced initial results from a multiple-dose, multi-center Phase II clinical study of ETC-216. The study met its primary efficacy objective of demonstrating statistically significant regression of atherosclerosis with ETC-216. The trial was a double-blind, placebo-controlled study evaluating the efficacy of ETC-216 at two different dose levels (15 mg/kg and 45 mg/kg), administered once weekly for a maximum of five treatments. The study included 47 evaluable patients with acute coronary syndromes who were scheduled to undergo coronary angiography and who continued to receive their current treatments during the study. Changes in plaque volume were measured using intravascular ultrasound, in which a tiny ultrasound probe is inserted into the coronary artery to directly image atherosclerotic plaques. The primary endpoint was the change in percent plaque volume for all evaluable patients receiving ETC-216 comparing end-of-treatment values to baseline values as measured with intravascular ultrasound. The results of this study demonstrated, for the first time in a clinical trial, statistically

significant regression of atherosclerosis at the end of six weeks.

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In June 2003, we announced the initiation of a multiple-dose, multi-center clinical study of ETC-642 in patients with stable cardiovascular disease. The primary objective of the study is to assess various potential dosing levels and regimens for ETC-642 while evaluating safety and tolerability. The study will also examine the pharmacokinetics and lipid effects of selected dosing regimens. The double-blind, placebo-controlled Phase I study will evaluate ETC-642 at up to four dose levels. Up to 32 patients with stable atherosclerosis will receive, in addition to their current treatments, either once-weekly doses of ETC-642 or placebo over the treatment period.

We recently initiated our first clinical trial for ETC-1001 in healthy volunteers. This trial is a double-blind, placebo-controlled trial designed to evaluate the safety and tolerability of single escalating doses of ETC-1001.

On July 16, 2003, we announced financial results for the three months ended June 30, 2003, reflecting a net loss of $8.4 million, or $0.29 per share. The net loss for the six months ended June 30, 2003 was $15.8 million, or $0.54 per share. Total operating expenses for the three months and six months ended June 30, 2003 were $7.8 million and $14.9 million, respectively.

Additional Information

We were incorporated in Delaware and commenced operations in July 1998. We became a public company in August 2000 and our common stock trades on The Nasdaq National Market under the symbol ESPR. Our executive offices and primary research facility are located at 3621 South State Street, 695 KMS Place, Ann Arbor, Michigan 48108; our telephone number is (734) 332-0506; and our website is http://www.esperion.com. The information on our website is not incorporated into, and does not constitute any part of, this prospectus.

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The Offering

Unless otherwise indicated, all of the information in this prospectus assumes no exercise of the underwriters over-allotment option to purchase up to an additional 434,000 shares of common stock from us and up to an additional 166,000 shares from the selling stockholders.

Common stock offered by us	4,000,000
Common stock to be outstanding after the offering	33,480,766
Use of proceeds	We currently intend to use the estimated net proceeds from this offering to fund our operations, for working capital and for general corporate purposes, including, capital expenditures, clinical development, partnership arrangements and in-licensing of technology. See Use of Proceeds.
Nasdaq National Market Symbol	ESPR

The number of shares of common stock to be outstanding after this offering is based on 29,480,766 shares outstanding as of June 30, 2003 and excludes:

- 3,987,175 shares of common stock underlying options outstanding as of June 30, 2003 at a weighted average exercise price of $6.52 per share; and
- 1,272,681 shares available for issuance or future grant under our 2000 Equity Compensation Plan, 169,989 shares available for issuance or future grant under our 1998 Stock Option Plan and 449,660 shares available for issuance under our Employee Stock Purchase Plan.

Summary Financial Data

The following data, insofar as they relate to each of the years 2000-2002, have been derived from annual financial statements, including the consolidated balance sheets at December 31, 2001 and 2002 and the related consolidated statements of operations and cash flows for the three years ended December 31, 2002 and the notes thereto, incorporated herein by reference. The data for the three months ended March 31, 2002 and 2003 have been derived from unaudited financial statements also incorporated herein by reference and which, in the opinion of management, include all adjustments, consisting only of normal recurring adjustments, necessary for a fair statement of the results for the unaudited interim periods.

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Consolidated Statement of Operations Data

	Year Ended December 31,			Three Months Ended March 31,	
	2000(1)	2001(1)	2002	2002	2003
	(in thousands, except share and per share data)			(unaudited)	
Operating expenses:					
Research and development	$22,596	$21,454	$21,991	$5,705	$5,460
General and administrative	3,156	5,023	5,955	1,645	1,629
Goodwill amortization(2)	250	839			
Purchased in-process research and development(3)	4,000				
Operating loss	(30,002)	(27,316)	(27,946)	(7,350)	(7,089)
Other income (expense), net	2,426	2,385	(780)	47	(317)
Net loss	(27,576)	(24,931)	(28,726)	(7,303)	(7,406)
Beneficial conversion feature(4)	(22,870)				

Net loss attributable to common stockholders	$(50,446)	$(24,931)	$(28,726)	$(7,303)	$(7,406)
Basic and diluted net loss per share(5)	$(4.50)	$(0.91)	$(0.98)	$(0.25)	$(0.25)
Shares used in computing basic and diluted net loss per share(5)	11,222,319	27,309,502	29,260,930	29,197,523	29,395,549
Pro forma basic and diluted net loss per share(5)	$(2.45)				
Shares used in computing pro forma basic and diluted net loss per share(5)	20,603,313				

Consolidated Balance Sheet Data

	December 31,		
	2001(1)	2002	March 31, 2003
	(in thousands)		(unaudited)
Cash, cash equivalents and short-term investments	$70,286	$44,853	$37,858
Working capital	64,926	40,330	33,490
Total assets	78,340	51,407	44,272
Long-term debt, less current portion	5,482	7,731	7,721
Deficit accumulated during the development stage	(65,320)	(94,046)	(101,452)
Total stockholders equity	66,498	38,743	31,593

(1) Arthur Andersen LLP audited our consolidated financial statements for periods prior to 2002. You should refer to the final risk factor under Risk Factors Risks Related to This Offering on page 14.

(2) SFAS No. 142, Goodwill and Other Intangible Assets, was adopted effective January 1, 2002. Net loss, net loss attributable to common stockholders and net loss and pro forma net loss per share adjusted to reflect the impact of SFAS No. 142 as if it had been adopted at the beginning of 2000 are $27.3 million, $50.2 million and $2.43 and $4.47; and net loss and net loss per share adjusted to reflect the impact of SFAS No. 142 as if it had been adopted at the beginning of 2001 are $24.1 million and $0.88.

(3) We recorded a $4.0 million charge to operations in 2000 for the write-off of purchased in-process research and development related to the acquisition of Talaria Therapeutics, Inc.

(4) We recorded approximately $22.9 million relating to the beneficial conversion feature of the Series C and Series D preferred stock in the first quarter of fiscal 2000 through equal and offsetting adjustments to additional paid-in-capital with no net impact on stockholders equity. The beneficial conversion feature was considered in the determination of our net loss attributable to common stockholders and net loss per share amounts.

(5) Basic and diluted net loss per share amounts have been calculated using the weighted average number of shares of common stock outstanding during the respective periods. Pro forma basic and diluted net loss per share amounts include the shares used in computing basic and diluted net loss per share and the assumed conversion of all outstanding shares of preferred stock from the original date of issuance.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should consider carefully the following risk factors, in addition to the other information in this prospectus, before making an investment decision. Each of these risk factors could adversely affect our business, operating results and financial condition, and the value of an investment in our common stock.

Risks Related to Our Company

We are a development stage biopharmaceutical company with a history of losses, and, even if our product candidates are approved and commercialized, we may never be profitable.

We have devoted substantially all of our resources since we began our operations in July 1998 to the research and development of product candidates for cardiovascular disease. We have incurred substantial losses since we began our operations. These losses have resulted principally from costs incurred in our research and development programs, from our general and administrative expenses and from acquisition-related costs from our September 2000 acquisition of Talaria Therapeutics, Inc. To date, we have not generated revenue from product sales or royalties, and we do not expect to achieve any revenue from product sales or royalties until we receive regulatory approval and begin commercialization of our product candidates. We are not certain of when, if ever, that will occur. We expect to incur significant additional operating losses for at least the next several years. Research and development costs relating to our product candidates will continue to increase. Manufacturing, sales and marketing costs will increase as we prepare for the commercialization of our product candidates.

All of our current product candidates are in early stages of development, and we face the risks of failure inherent in developing drugs based on new technologies. Because our product development strategy is predicated on a novel treatment approach based upon our understanding of HDL, we have limited in-house experience with our product candidates. Our product candidates are not expected to be commercially available for several years, if at all.

The technology underlying our product candidates is uncertain and unproven, which could keep our product candidates from becoming commercially successful.

All of our current product development efforts are based on unproven technology and therapeutic approaches that have not been widely tested or used or approved for marketing in any country. To date, no products that use our technology have been commercialized. If our product candidates do not work as intended, or if the data from our clinical trials indicate that our product candidates are not safe and effective, the applicability of our technology for treating cardiovascular disease will be highly uncertain. For example, the future of ETC-216 may be called into question and the market price of our common stock could decline if the information that we ultimately release about the recently completed ETC-216 trial with respect to the patients who did not receive ETC-216 suggests that ETC-216 will not produce a statistically significant regression of atherosclerosis as compared to the current treatment for acute coronary syndromes. In June 2003, we announced initial results from this trial that demonstrated statistically significant regression of atherosclerosis at the end of six weeks. We did not announce, however, the results of plaque volume measurements taken at the beginning and end of a six-week period in the limited number of patients in the trial who did not receive ETC-216 but who continued to receive their current treatments. We have not released this information publicly yet because the primary endpoint of the trial was not designed to compare the results of this non-treatment group with the treatment groups, and because of our need to comply with non-disclosure rules applied by medical journals, including those to which the manuscript of this study might be submitted. Even if the information that we ultimately release with regard to the non-treatment group is not inconsistent with the recently announced

favorable initial trial results, this would not mean that ETC-216 would reduce the number of clinical events resulting from cardiovascular disease. As a result, there is a significant risk that our therapeutic approaches will not prove to be successful, and there can be no guarantee that our drug discovery technology will result in any commercially successful products.

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All of our product candidates must be tested and submitted to the FDA and foreign regulatory agencies for approval before we can sell them in the United States or other countries, and even if our product candidates receive regulatory approval, that approval may be limited, which would hinder our ability to commercialize them.

Our product candidates must satisfy rigorous standards of safety and efficacy before they receive regulatory approval in the United States and other countries. We will need to conduct significant additional research, including additional pre-clinical testing involving animals and clinical trials involving humans, before we can file applications for product approval.

Many of the product candidates in the pharmaceutical and biopharmaceutical industries do not successfully complete pre-clinical testing and clinical trials. Satisfaction of regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product and requires the expenditure of substantial resources. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful. For example, a number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials and in interim analyses. In addition, delays or rejections may be encountered based upon additional government regulations, including any changes in FDA policy, during the process of product development, clinical trials and regulatory approvals.

In order to receive regulatory approval from U.S. or foreign regulatory authorities to market a product, we must demonstrate through human clinical trials that the product candidate is safe and effective for the treatment of a specific condition. Even if we believe that the clinical trials demonstrate safety and efficacy of a product, the FDA and foreign regulatory authorities may not accept our assessment of the results and may require us to conduct additional advanced clinical trials.

Approval of a product by applicable regulatory authorities is necessary in foreign countries prior to the commencement of marketing of the product in those countries, whether or not U.S. regulatory approval has been obtained. The approval procedure varies among countries and can involve additional testing. The time required may differ from that required for U.S. regulatory approval. Although there are some procedures for unified filings for some European countries with the sponsorship of the country that first granted marketing approval, in general, each country has its own procedures and requirements, many of which are time consuming and expensive.

We do not know whether planned clinical trials will begin on time or will be completed on schedule or at all. If we experience significant delays in testing or approvals, or if we need to perform more or larger clinical trials than planned, our product development costs will increase. Any of our future clinical studies might be delayed or halted because the drug is not safe and effective, or physicians think that the drug is not safe or effective; patients do not enroll in the studies at the rate we expect; or drug supplies are not sufficient to treat the patients in the studies.

Any regulatory approvals in the United States that we receive in the future could also include significant restrictions on the use or marketing of any future products. Product approvals, if granted, can be withdrawn for failure to comply with regulatory requirements or upon the occurrence of adverse events following commercial introduction of the products.

If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop our product candidates or retain rights to our product candidates.

Significant additional capital will be required in the next several years to fund our operations. Excluding the proceeds of this offering, our current available capital is only sufficient to fund our operations into the second half of 2004. We do not know whether additional financing will be available on acceptable terms when needed. We have used substantial cash resources to date and expect capital outlays

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and operating expenditures to increase over the next several years as we expand our infrastructure and research and development activities. If adequate funds are unavailable, we may be required to:

- delay, reduce the scope of or eliminate one or more of our research or development programs;
- license rights to our technology or product candidates on terms that are less favorable to us than might otherwise be available; or
- obtain funds through arrangements that may require us to relinquish rights to all or some of our product candidates that we would otherwise seek to develop or commercialize ourselves.

Our freedom to operate our business or profit fully from any sales of our future products may be limited depending upon the terms of any collaborative agreements into which we enter, and the inability to establish one or more collaborative arrangements could adversely affect our ability to develop and commercialize products.

We are seeking to collaborate with pharmaceutical companies to gain access to their drug development, regulatory, manufacturing, marketing, sales and financial resources. However, we may not be able to negotiate arrangements with partners on favorable terms, if at all, or enter into collaborations that will be commercially successful. Our ability to enter into collaborative arrangements relating to less than all of our biopharmaceutical product candidates may be adversely affected by the similarities among those product candidates. Any collaborative relationships that we enter into may include restrictions on our freedom to operate our business or may limit any sales of our future products. If a collaborative arrangement is established, the collaborative partner may discontinue funding any particular program or may, either alone or with others, pursue alternative technologies or indications or develop alternative product candidates for the diseases we are targeting. Competing products, developed by a collaborative partner or to which a collaborative partner has rights, may result in the collaborative partner withdrawing support as to all or a portion of our technology.

Our ability to enter into a collaborative arrangement for ETC-216 may be limited by the terms of our agreement with Pharmacia Corporation. Pharmacia has the right to co-develop and exclusively market ETC-216 outside the United States and Canada once we complete Phase IIb clinical trials and a right of first negotiation if we wish to pursue a co-development and co-promotion arrangement in the United States and Canada. If Pharmacia does not exercise its right to co-develop and market ETC-216 outside the United States and Canada, or if it does not choose to participate in co-development and co-promotion within the United States and Canada, other potential partners may not be willing to enter into an agreement relating to ETC-216. If we decide to seek a co-development and co-promotion arrangement in the United States and Canada prior to completion of Phase IIb clinical trials and Pharmacia does not respond to our request that they advise us whether they want to exercise their right of first negotiation, we may need to agree to indemnify our partner from any claims made by Pharmacia that we have breached our agreement with it.

Without collaborative arrangements, we must fund our own research, development, manufacturing, marketing and sales activities, which would accelerate the depletion of our cash and require us to raise substantial additional cash to enable us to develop our own development, regulatory, manufacturing, marketing and sales capabilities. Therefore, if we are unable to establish and maintain satisfactory collaborative arrangements and if other sources of cash are not available, we could experience a material adverse effect on our ability to develop products and, if developed and approved, to manufacture, market and sell them successfully.

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We expect our quarterly and annual results to fluctuate significantly.

During the next several years, we expect our quarterly and annual operating results to fluctuate significantly, depending primarily on the following factors:

- timing of pre-clinical studies and clinical trials;
- interruptions or delays in the supply of our product candidates or components;
- timing of payments to licensors and other third parties;
- whether we enter into collaboration agreements and the timing and accounting treatment of payments, if any, to us under those agreements;
- timing of patent prosecution and maintenance fees and costs;
- timing of investments in new technologies; and
- other costs, which may be unexpected.

If the third-party clinical research organizations that we rely on to conduct our clinical trials do not perform in an acceptable and timely manner, or if we are not able to manage or administer multiple clinical trials simultaneously, our clinical trials could be delayed, halted or unsuccessful, and we could be unable to commercialize our product candidates on a timely basis, if at all.

We do not currently have the ability to independently conduct clinical trials and obtain regulatory approvals for our product candidates, and we currently rely and intend to continue to rely on third-party clinical investigators and contract research organizations to perform these functions. If we cannot locate acceptable contractors to run our clinical trials or enter into favorable agreements with them, or if these third parties do not successfully carry out their contractual duties or meet expected deadlines, we will be unable to obtain required approvals and will be unable to commercialize our product candidates on a timely basis, if at all.

Our clinical studies may also be limited by, delayed or halted because of the nature of the clinical study; the size of the potential patient population; the distance between patients and the clinical trial sites; the number of trials utilizing the same patient population; delays in enrolling patients; or the eligibility and exclusion criteria for patients in the trial.

To date, we have not managed multiple late-stage clinical trials simultaneously. As of June 30, 2003, we have completed six clinical trials (two of which were conducted through a company that we acquired) and have five clinical trials in progress. It may be difficult or we may be unable to retain individuals qualified to administer these and future late-stage clinical trials due to the complexity of the protocols and the size of the studies. We may be unable to complete multiple late-stage clinical trials concurrently as effectively or as quickly as we currently anticipate, which could have a material adverse effect on our business, financial condition and results of operations.

If our current and future manufacturing and supply strategies are unsuccessful, we may be unable to complete any future clinical trials or commercialize our product candidates in a timely manner, if at all.

Completion of our clinical trials and commercialization of our product candidates will require access to, or development of, facilities to manufacture a sufficient supply of our product candidates. We do not have the resources, facilities or experience to manufacture our product candidates on our own and do not intend to develop or acquire facilities for the manufacture of product candidates for clinical trials or commercial purposes in the foreseeable future. We currently rely, and will continue to rely, on contract manufacturers to produce sufficient quantities of our product candidates. We are currently exploring ways to improve the manufacturing process for our ETC-216 product candidate, as the yield from the current process will need to be enhanced in order to meet late-stage clinical trial supply and commercial-scale requirements. If we are unable to improve the current manufacturing process, we may be unable to complete future clinical trials for, or to cost-effectively commercialize, this product candidate. Most of our

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contract manufacturers have limited experience with manufacturing, formulating, analyzing, filling and finishing our particular product candidates. Our manufacturing strategy presents the following difficulties:

- we may not be able to locate acceptable manufacturers or enter into favorable long-term agreements with them;
- third parties may not be able to manufacture our product candidates successfully in a cost-effective or timely manner or in quantities needed for clinical trials or commercial sales;
- delays in, or failures to achieve, scale-up to commercial quantities, or changes to current raw material suppliers or product manufacturers (whether the change is attributable to us or the vendor) could delay clinical studies, regulatory submissions and commercialization of our product candidates;
- we may not have intellectual property rights, or may have to share intellectual property rights, to the manufacturing processes for our product candidates;
- manufacturing and validation of manufacturing processes and materials are complicated and time-consuming and may not provide yields adequate to meet clinical trial supply or commercial scale-up requirements;
- because many of our current third-party manufacturers are located outside of the United States, there may be difficulties in importing our product candidates or their components into the United States as a result of, among other things, FDA import inspections, increased customs security measures, incomplete or inaccurate import documentation, or defective packaging; and
- manufacturers of our product candidates are subject to the FDA s current Good Manufacturing Practices regulations, the FDA s current Good Laboratory Practices regulations and comparable foreign standards and we do not have control over compliance with these regulations by our third-party manufacturers.

If any manufacturer of our product candidates fails to comply with applicable FDA or other regulatory requirements including manufacturing, quality control, labeling, safety surveillance, promoting and reporting, such failure may result in our criminal prosecution, levy of civil penalties against us, recall or seizure of any of our future products, total or partial suspension of production or an injunction, as well as other regulatory actions against our manufacturers, our potential products or us. Discovery of previously unknown problems with a product, supplier, manufacturer or facility may result in restrictions on the sale of a future product, including a withdrawal of the product from the market.

If one of our biopharmaceutical product candidates does not show safety and efficacy in early clinical trials, it could impact the development path for our other biopharmaceutical product candidates because of the similarities in the technology for each of our biopharmaceutical product candidates.

The development of each of our biopharmaceutical product candidates (ETC-588, ETC-216 and ETC-642) is based on our knowledge and understanding of HDL and how HDL contributes to the RLT pathway. While there are important differences in each of the product candidates in terms of their composition and properties, each product candidate is focused on affecting various steps in the RLT pathway. In addition, all three of the biopharmaceutical product candidates are infused, rather than orally administered, and are currently being targeted for the treatment of patients with acute coronary syndromes.

As a result of these similarities, our product candidates may be perceived to have overlapping utility in the treatment of cardiovascular disease. Since we are developing these product candidates in parallel, we expect to learn from the results of each trial and apply some of our findings to the development of the other product candidates. If one of the product candidates has negative clinical trial results or is shown to be ineffective, it could impact the

development path or future development of the other biopharmaceutical product candidates. If we find that one of the biopharmaceutical product candidates is unsafe, we may be unable to raise sufficient capital to fund the development of the other biopharmaceutical product

candidates due to any resultant negative perceptions about HDL as an infused, acute treatment for cardiovascular disease.

If we fail to secure and enforce patents and other intellectual property rights underlying our product candidates and technology, we may be unable to develop our product candidates or compete effectively.

The pharmaceutical and biopharmaceutical industries place considerable importance on obtaining patent and trade secret protection for new technologies, products and processes. Our success will depend, in part, on our ability, and the ability of our licensors, to obtain and enforce our exclusive rights to our product candidates and technology under the patent laws of the United States and other countries. Our success also will depend on our ability to prevent others, including our employees, from using our trade secrets, know how and other confidential information. In addition, we must operate in a way that does not infringe, or violate, the patent, trade secret and other intellectual property rights of other parties.

The standards that the United States Patent and Trademark Office uses to grant patents can change. Consequently, we may be unable to determine the type and extent of patent claims that will be issued to us or to our licensors in the future. Any patents issued may not contain claims that will permit us to stop competitors from using the same or similar technology.

Patent prosecution and maintenance are also very costly and successful prosecution and defense may depend on the patent strategies that are pursued.

The standards that courts use to interpret patents can change, particularly as new technologies develop. Consequently, we cannot know how much protection, if any, our patents will provide. If we choose to seek a court order that prohibits a third party from using the inventions claimed in our patents, the third party may ask the court to rule that our patents are invalid and unenforceable. This type of lawsuit is expensive and time consuming and could be unsuccessful. There is also the risk that, even if the validity of our patents is upheld, the court will refuse to stop the third party on the ground that its activities do not infringe the patent.

If our licensing arrangements with third parties are breached or terminated, we may lose rights to commercialize our product candidates.

We license most of the technology for our biopharmaceutical product candidates from third parties. We depend, and will continue to depend, on these and other licensing arrangements. If any of our licenses with third parties are terminated or breached, we may lose our rights to develop and commercialize our product candidates or lose patent or trade secret protection for our product candidates.

Disputes may arise with respect to our licensing agreements and strategic relationships regarding ownership rights to technology developed by or with other parties or with respect to manufacturing, development and other strategies and decisions. Such disputes could lead to delays in or termination of the research, development, manufacture and commercialization of our product candidates, or to litigation.

We may face significant expense and liability as a result of litigation or other proceedings relating to patents and other intellectual property rights of third parties, which could reduce our available capital.

If third parties file patent applications, or are issued patents, claiming technology also claimed by us or our licensors in pending applications or issued patents, we may be required to participate in interference proceedings in

the United States Patent and Trademark Office to determine priority of invention. An adverse outcome in an interference proceeding could require us to forfeit our patents or applications involved in the interference, cease using the technology or license rights from prevailing third parties. We could also be subject to allegations of trade secret violations and other claims relating to the intellectual property rights of third parties.

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If product liability lawsuits are successfully brought against us, we may incur substantial liabilities and may be required to limit commercialization of any of our future products.

Our business exposes us to product liability risks that are inherent in the clinical testing, manufacturing, marketing and sale of pharmaceutical and biopharmaceutical products. We may not be able to avoid product liability claims. Product liability insurance for the pharmaceutical and biopharmaceutical industries is generally expensive, if available at all. We have clinical trial liability insurance for our product candidates in clinical trials; however, there can be no assurance that such insurance coverage is or will continue to be adequate or available. We may not be able to secure greater or broader product liability insurance coverage on acceptable terms or at reasonable costs when needed. If we are unable to obtain sufficient insurance coverage on reasonable terms or to otherwise protect against potential product liability claims, we may be unable to commercialize our product candidates. A successful product liability claim brought against us for damages in an amount that exceeds our insurance coverage, if any, may cause us to incur substantial liabilities and our business may fail.

If our competitors develop and commercialize products faster than we do or commercialize products that are superior to our product candidates, our commercial opportunities will be reduced or eliminated.

The extent to which any of our product candidates achieve market acceptance will depend on competitive factors, many of which are beyond our control. Competition in the pharmaceutical and biopharmaceutical industries is intense and has been accentuated by the rapid pace of technology development. Our competitors include large fully-integrated pharmaceutical companies, biopharmaceutical companies, biotechnology companies, universities and public and private research institutions. Many of these entities have substantially greater research and development capabilities and financial, scientific, manufacturing, marketing and sales resources than we do, as well as more experience in research and development, clinical trials, regulatory matters, manufacturing, marketing and sales. These organizations also compete with us to:

attract parties for collaborations, joint ventures or acquisitions;

license the proprietary technology that is competitive with our technology;

attract funding; and

attract and hire scientific talent.

Our competitors may succeed in developing and commercializing products earlier, and obtaining regulatory approval more rapidly, than we do. Our competitors may also develop products or technologies that are superior to those we are developing, and render our product candidates or technology obsolete or non-competitive. If we cannot successfully compete with new or existing products, our marketing and sales would suffer and we may not ever be profitable.

Our product candidates may not be commercially successful because physicians, patients and government agencies and other third-party payors may not accept them.

Even if regulatory authorities approve our product candidates, they may not be commercially successful. Third parties may develop superior products or less costly alternative products, or have proprietary rights that preclude us from marketing any of our future products. We also expect that most of our product candidates will be considered expensive, if approved. Patient acceptance of and demand for any product candidates for which we obtain regulatory approval will also depend upon acceptance by physicians of any of our product candidates as safe and effective therapies and the extent, if any, of reimbursement of drug and treatment costs by government agencies and other

third-party payors.

In addition, any of our product candidates could cause adverse events, such as immunologic or allergic reactions. These reactions may not be observed in clinical trials, but may nonetheless occur after commercialization. If any of these reactions occur, they may render any commercialized product ineffective in some patients and thereby hinder the sales of such product.

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Our failure to obtain an adequate level of reimbursement or acceptable prices for any of our future products could diminish any revenues we may be able to generate.

Our ability to commercialize any future products successfully, alone or with collaborators, will depend in part on the extent to which reimbursement for the products will be available from:

government and health administration authorities;

private health insurers; and

other third-party payors.

Government and other third-party payors increasingly are attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for new drugs. Third-party private health insurance coverage may not be available to potential patients for any of our future products.

The continuing efforts of government and other third-party payors to contain or reduce the costs of healthcare through various means may limit our commercial opportunity and reduce any associated revenue and profits. We expect proposals to implement similar government control to continue. In addition, increasing emphasis on managed care will continue to put pressure on the pricing of pharmaceutical and biopharmaceutical products. Cost control initiatives could decrease the price that we or any potential collaborators could receive for any of our future products and could adversely affect our profitability. In addition, in some countries other than the United States, pricing and profitability of prescription pharmaceuticals and biopharmaceuticals are subject to government control.

Even if we obtain regulatory approval of any of our product candidates, we will not be able to successfully commercialize such product candidates if we are unable to create sales, marketing and distribution capabilities or enter into appropriate collaborative arrangements.

In order to commercialize any of our product candidates successfully, we must either internally develop full and efficient sales, marketing and distribution capabilities or make arrangements with third parties to perform these services. We have no experience in developing, training or managing a sales force and will incur substantial additional expenses in doing so. The cost of establishing and maintaining a sales force may exceed its cost effectiveness. In addition, we will compete with many companies that currently have extensive and well-funded marketing and sales operations. Our marketing and sales efforts may be unable to compete successfully against these companies.

If we fail to recruit, retain and motivate skilled personnel, our product development programs, our research and development efforts and the release of our product candidates may be delayed.

Our success depends on our ability to recruit, retain and motivate highly-qualified management and scientific personnel, including skilled chemists and clinical development personnel, for which competition is intense. Our loss of the services of any of our key personnel, in particular, Roger S. Newton, Ph.D., our President and Chief Executive Officer, could significantly impede the achievement of our research and development objectives and could delay our product development programs and strategies.

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

Our research and development activities involve the controlled use of potentially harmful biological materials as well as hazardous materials, chemicals and various radioactive compounds. We cannot completely eliminate the risk

of accidental contamination or injury from the use, storage, handling or disposal of these materials. In the event of contamination or injury, we could be held liable for damages, and such liability could exceed our resources. We are subject to federal, state, local and international laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. The cost of compliance with these laws and regulations could become significant.

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Risks Related to This Offering

Our common stock price has been volatile and could experience a substantial decline in value.

The market price of our common stock has historically experienced and may continue to experience volatility. During the 12 months ended June 30, 2003, the market price of our common stock ranged from $4.15 to $19.80 per share. Our quarterly operating results, announcements of collaborations, the success or failure of the drug development efforts of our collaborators, technological innovations being developed by us or our competitors, changes in general conditions in the economy or the financial markets and other developments affecting our competitors, our collaborators or us could cause the market price of our common stock to fluctuate substantially. In addition, in recent years, the stock market in general, and the market for pharmaceutical and biopharmaceutical companies in particular, have experienced significant price and volume fluctuations. This volatility has affected the market prices of securities issued by many companies, often for reasons unrelated to their operating performance, and may adversely affect the price of our common stock. In the past, securities class action litigation has often been instituted following periods of volatility in the market price of a company s securities. A securities class action suit against us could result in potential liabilities, substantial costs and the diversion of management s attention and resources, regardless of whether we win or lose.

New investors in our common stock will experience immediate and substantial dilution.

The offering price to the public is substantially higher than the book value per share of our common stock. Investors purchasing common stock in this offering will, therefore, incur immediate dilution of $16.89 in net tangible book value per share of common stock, based on an estimated offering price to the public of $20.00 per share. Investors may incur additional dilution upon the exercise of outstanding stock options and warrants.

Our share ownership is concentrated, and our officers, directors and principal stockholders may exert significant control over our business and matters requiring stockholder