EMISPHERE TECHNOLOGIES INC
Form 424B3
December 06, 2005

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Registration No. 333-129891

Prospectus

50,000 shares

Common Stock

This prospectus relates to the resale of up to 50,000 shares of our common stock issued or issuable upon exercise of options that we issued to the selling shareholder named in this prospectus. The selling shareholder will receive all of the proceeds from the sale of shares of common stock hereunder. We will receive the proceeds from any cash exercise of the options by the selling shareholder. We will bear the costs relating to the registration of the shares of common stock, which we estimate will be approximately $30,000.

The selling shareholder may offer its shares through public or private transactions on or off the Nasdaq National Market at prevailing market prices or at privately negotiated prices. The selling shareholder may make sales directly to purchasers or through brokers, agents, dealers or underwriters or through a combination of these methods. The selling shareholder will bear all commissions and other compensation paid to brokers in connection with the sale of its shares.

Our common stock is traded on the Nasdaq National Market under the symbol EMIS. On December 2, 2005, the last reported sale price for our common stock on the Nasdaq National Market was $4.65 per share.

Investing in our common stock involves significant risks. See Risk Factors beginning on page 8.

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.

The date of this Prospectus is December 6, 2005.

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We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus. This prospectus does not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor does this prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. The information contained in this prospectus is accurate as of the date on its cover. When the selling shareholder delivers this prospectus or makes a sale pursuant to this prospectus, there is no implication that the information is current as of the date of the delivery or sale.

Unless the context otherwise requires, the terms we, our, us, the Company and Emisphere refer to Emisphere Technologies, Inc.

PROSPECTUS SUMMARY

You should read the following summary together with the more detailed information, including the consolidated financial statements and the notes to the consolidated financial statements and other information, included, or incorporated by reference, in this prospectus.

OUR COMPANY

Overview

Emisphere Technologies, Inc. is a biopharmaceutical company developing products using its proprietary *e*lig*e*n® drug delivery technology. We apply this technology to orally administer therapeutic macromolecules that are not currently available in oral form. We believe that our drug delivery technology may lead to greater patient convenience and compliance, and in some cases, improved therapies. As of September 30, 2005, we have 81 patents issued and 57 applications pending in the United States, and patent and patent applications covering product candidates in the anticipated markets for such products.

We have product candidates in development across a broad range of therapeutic areas, including cardiovascular disease, diabetes, osteoporosis, growth disorders, asthma and allergies, obesity and infectious diseases. Also, we have partnerships with world-leading pharmaceutical companies. To date, we have devoted substantially all of our efforts and resources to research and development and have not generated sales of any of our products. For more information about our financial condition and prospects, please refer to the section entitled Certain Other Recent Developments below.

Oral Drug Delivery

The pharmaceutical industry has been working for many years to overcome the challenge of delivering therapeutic macromolecules orally, with limited success. Therapeutic macromolecules are comprised of proteins and other large molecules that, if ingested, would degrade in the stomach or intestine before they are absorbed into the bloodstream. Therefore, they are administered by injection or by intravenous means (collectively referred to as parenteral administration or parenterally). Parenteral administration is believed to be less desirable than oral administration for many reasons, including patient discomfort, inconvenience and risk of infection. In addition, parenteral therapies often include the cost of administration by a healthcare professional, since they typically require administration in hospitals or doctors offices. Poor patient acceptance of, and compliance with, parenteral therapies can lead to increased incidences of medical complications.

Our business strategy is based upon our belief that the development of an efficient and safe oral delivery system for therapeutic macromolecules that are currently administered parenterally represents a significant commercial opportunity. We believe that, given the choice, patients reluctant to commence or comply with parenteral therapies would embrace an oral alternative, thus spurring market expansion for therapeutic macromolecules.

Our Technology

Our oral delivery technology, the *e*lig*e*n® technology, is based upon proprietary, synthetic chemical compounds, that we refer to as EMISPHERE® delivery agents (or carriers), which facilitate the transport of therapeutic macromolecules across biological membranes, such as the membranes of the small intestine. We believe that the *e*lig*e*n® technology uses a natural transport process in the body to accomplish this objective. Our hypothesis is that EMISPHERE® delivery agents change the shape of the macromolecule without changing its chemical composition, and that the changed shape allows the macromolecule to cross the membrane. Once the therapeutic macromolecule crosses the membrane, the EMISPHERE® delivery agent separates from the macromolecule, which then reestablishes its natural shape, allowing it to remain therapeutically active. Using this technology, we have orally delivered heparin, low molecular weight heparin, insulin, PTH 1-34, rhGH, salmon calcitonin, a small molecule compound and cromolyn in humans and over 40 other compounds in laboratory animals.

Competitive Advantages

We believe that the *e*lig*e*n® technology has competitive advantages, including:

EMISPHERE® delivery agents are applicable across a diverse group of molecules such as proteins, peptides, carbohydrates, polar organics and other compounds;

Oral drug delivery using the *e*lig*e*n® technology does not rely upon the addition of other agents that can have adverse effects on the intestinal membranes or digestion;

EMISPHERE® delivery agents are adaptable to various types of oral formulations, including solutions, suspensions, tablets and capsules; and the technology may be compatible with controlled release dosage forms; and

We believe that the technology and manufacturing equipment required to produce EMISPHERE® delivery agent material in commercial quantities is readily available.

We have research and development collaborations and licensing agreements with corporate partners to provide development and commercialization services relating to certain of our products under development. Under these agreements, we have granted licenses or the rights to obtain licenses to our oral drug delivery technology. In return, we are entitled to reimbursement for research and development costs that we incur, payments upon the achievement of milestones, and royalties on the sales of successfully commercialized products.

Lead Product Candidates

Oral Heparin

Heparin is an anti-coagulant/anti-thrombotic used to prevent blood clots (deep vein thrombosis or DVT) following major surgical procedures lasting longer than 30 minutes. According to the website www.dvt.org (maintained by the University of Massachusetts Medical School), the risk of developing DVT following major surgery can range as high as seventy percent. Recent studies published in *The Lancet* and the *Journal of Bone and Joint Surgery* support longer term use of heparin for prophylaxis to cover the high-risk periods for forming blood clots following major surgery. Published reports that we refer to below also suggest that unfractionated heparin (UFH) may have utility for indications other than anti-coagulation and anti-thrombosis. We believe that potential longer term use of heparin as a prophylaxis and other potential indications for unfractionated heparin could present opportunities for our solid oral heparin and low molecular weight heparin candidates.

On the basis of our extensive clinical testing with a liquid form of oral UFH, we believe we are well positioned to rapidly bring forward a new solid formulation into late-stage clinical trials. In the first quarter of 2004, we selected tablet and capsule prototypes for production and clinical testing in the United States. In June 2004, we completed a Phase I clinical trial to evaluate these tablet and capsule dosage forms. In August 2004, we announced that we selected a soft gelatin capsule formulation of UFH based on the results of the Phase I trial. We are currently seeking U.S. Food and Drug Administration (FDA) approval to begin Phase III testing. Later stage clinical trials may not support the findings of our early stage trials.

Oral Insulin

Injectable insulin is widely used in the treatment of Type 1 and Type 2 diabetic patients. According to the publicly filed annual reports of the leading insulin manufacturers, worldwide sales of insulin exceeded $5.8 billion in 2003. Approximately 40% of all Type 2 diabetics use insulin to control the disease, accounting for approximately 50% of total insulin use. Although many more Type 2 diabetics could benefit from insulin therapy, use of the drug has been limited because it is administered by injection. We believe that a successful oral insulin therapy would facilitate compliance for diabetic patients who are not diligent with their prescribed injection regimens, and enable those patients adverse to injections to adopt insulin therapy at an earlier stage of the disease.

Because we believe that an oral form of insulin, if approved, would gain significant market share, we have focused significant resources on its development. Most recently, we have developed a tablet dosage form of insulin for oral administration that was tested in a 13-patient Phase I clinical trial designed to provide information related to efficacy, not effectiveness, completed in January 2004. Data from this trial indicated that repeated administration of our oral insulin was not associated with clinically relevant hypoglycemic events, an adverse complication that is often associated with injected insulin and other anti-diabetic treatments. There were no adverse events attributable to the study drug. Patients receiving EMISPHERE oral insulin tablets experienced a statistically significant drop from baseline in average blood glucose levels as measured by fructosamine levels, a statistically significant drop in fasting blood glucose levels and a statistically significant drop in glucose excursions following an oral glucose tolerance test. We presented an analyzed data set from this trial at the Annual Meeting of the American Diabetes Association in June 2004. Later stage clinical trials may not support the findings of our early stage trials.

Oral Salmon Calcitonin

We are collaborating with Novartis AG (Novartis) to develop oral salmon calcitonin (sCT), a peptide used to treat osteoporosis. sCT is currently available as an injection or nasal spray. In February 2003, we announced favorable results of a Phase IIa study conducted by Novartis evaluating the performance of an oral tablet form of sCT in post-menopausal women. Novartis has indicated to us that it intends to commence pivotal studies for two indications in the early part of 2006. Later stage clinical trials may not support the findings of our early stage trials.

Oral PTH 1-34

We have granted Novartis an option to license our technology for the development of an oral recombinant parathyroid hormone (PTH 1-34), a compound that stimulates new bone formation and is used for the treatment of osteoporosis. We previously partnered this program with Eli Lilly and Company (Lilly), and Lilly currently markets PTH 1-34 as an injectable drug. The Emisphere/Lilly oral PTH 1-34 program successfully completed Phase I studies and Lilly was responsible for trial management and funding. We are in litigation with Lilly concerning, among other things, an alleged violation by Lilly of the research and collaboration agreements relating to PTH 1-34 and we have given Lilly notice of our termination of those agreements. Emisphere has agreed to continue to provide Lilly with technical information as needed pending resolution of the court proceedings.

Oral rhGH

On September 23, 2004, we entered into a collaboration with Novartis to develop an oral formulation of recombinant human growth hormone (rhGH). We formed the agreement following the successful completion of pre-clinical feasibility studies for rhGH with our *e*lig*e*n® technology. We have identified delivery agents that can deliver therapeutically sufficient levels of rhGH to the bloodstream when administered orally. The lead carrier for rhGH has completed extensive formulation and pre-clinical safety studies. We will work with Novartis to initiate clinical trials of a convenient oral human growth hormone product using the *e*lig*e*n® technology. Novartis will fully fund the program including all clinical studies. Under the terms of the agreement, Novartis paid us an initial non-refundable fee of $1 million in exchange for a 12 month license to utilize our *e*lig*e*n® technology. In November 2005, we agreed to extend the initial 12 month license period until March 31, 2006. At the end of this period, Novartis has 30 days in which to elect to commence development or to terminate the agreement. If they elect to commence development, we may receive up to $33 million in additional milestone payments during the course of product development, and royalties based on sales.

Oral Small Molecule Compounds

On November 17, 2004, we entered into a licensing agreement with Hoffmann-La Roche Inc. and F. Hoffman-La Roche LTD (collectively, Roche) to develop oral formulations of undisclosed small molecule compounds approved for use in the field of bone-related diseases. The agreement follows successful pre-clinical studies and a human feasibility study incorporating our *e*lig*e*n® technology to treat bone disease. Later stage trials may not support the findings of our pre-clinical or feasibility studies. Roche will fund all necessary preclinical, clinical and manufacturing costs for all products. We have no payment obligations with respect to this program; we are, however, obligated to collaborate with Roche by providing access to our technology that is relevant to this program and are obligated to help manage this program through a joint steering committee with Roche. Under the terms of the agreement, Roche paid us an initial non-refundable up-front fee of $2.5 million in December 2004 and a milestone payment of $1.5 million

for the first product in June 2005. Roche may pay us future milestone payments of up to $17 million for the first product and $18.5 million each additional product developed using our *eligen*® technology. We may also receive royalties based on product sales. Given that the agreement with Roche was entered into in November 2004, there has not yet been sufficient time to achieve material scientific progress or development in connection with the activities to be undertaken under the agreement. Roche may terminate the agreement at will for any reason and without financial penalty or requirement to fund any further clinical studies. We retain ownership rights to developments relating to our carrier and Roche retains rights related to the drug product developed.

Other Collaborations and Feasibility Programs

In addition to the lead product candidates described above, we have product candidates utilizing charged molecules as well as macromolecules in various stages of development, either alone or with partners, which have the potential to address large underserved patient populations.

Certain Other Recent Developments

As of September 30, 2005, our accumulated deficit was approximately $341 million. Our net loss was $37.5 million and $44.9 million for the years ended December 31, 2004, and 2003 respectively. Net loss was $8.9 million for the nine months ended September 30, 2005. The significant decrease in net loss is a result of the $14.7 million gain on the extinguishment of the Elan note payable. Our cash outlays from operations and capital expenditures were $21.4 million for the first nine months of 2005 and $23.5 million for 2004. Our stockholders equity decreased from $67.5 million as of December 31, 2002 to a deficit of $5.9 million as of September 30, 2005. We have limited capital resources and operations to date have been funded with the proceeds from collaborative research agreements, public and private equity and debt financings and income earned on investments. These conditions raise su bstantial doubt about our ability to continue as a going concern. The audit report prepared by our independent registered public accounting firm relating to our consolidated financial statements for the year ended December 31, 2004 includes an explanatory paragraph expressing the substantial doubt about our ability to continue as a going concern.

As of September 30, 2005, we had cash, cash equivalents, restricted cash and investments totaling $18.3 million. As discussed below, the proceeds from this agreement are subject to certain restrictions imposed by the debt holder. We anticipate that our existing capital resources, without implementing cost reductions, raising additional capital, or obtaining substantial cash inflows from potential partners for our products, will not enable us to continue operations past March of 2006, or earlier if unforeseen events or circumstances arise that negatively affect our liquidity. These circumstances may adversely affect our ability to raise additional capital. If we fail to raise additional capital or obtain substantial cash inflows from potential or existing partners, we will be forced to cease operations. If additional capital is raised through the sale of equity or convertible debt securities, the issuance of such securities would result in dilution to our existing stockholders. We are continuing to address our liquidity issues through various means including the financing matters discussed below.

On September 26, 2005, we executed a Senior Secured Loan Agreement (the Loan Agreement) with MHR Institutional Partners IIA LP (together with certain affiliated funds, MHR). The Loan Agreement was amended on November 11, 2005 to clarify certain terms. The Loan Agreement provides for a seven year, $15 million secured loan from MHR to us at an interest rate of 11% (the Loan). Net proceeds from the loan were approximately $12.9 million. The Loan is secured by a first priority lien in favor of MHR on substantially all of our assets. The proceeds from the Loan were disbursed to a restricted account and our right to have such funds disbursed to an operating account is conditioned upon the requested amounts for any period not being in excess of 103% of amounts in our budget for such period (then in effect under the terms of the Loan Agreement), and provided that we certify to MHR that no event of default has occurred under the Loan Agreement (or the Convertible Note described below, as applicable), no material adverse change has occurred and our representations and warranties under the Loan Agreement continue to be true and correct. The Loan Agreement requires us to hold a special stockholder meeting as soon as practicable, but not later than December 25, 2005, for the purpose of obtaining

stockholder approval of (i) the exchange of the Loan for an 11% senior secured convertible note (the Convertible Note) with substantially the same terms as the Loan Agreement, except that the Convertible Note will be convertible, at the sole discretion of MHR or any assignee thereof, into shares of our common stock (the Conversion Shares) at a price per share of $3.78, interest will be payable in kind rather than in cash and we will have the right to call the Convertible Note after September 26, 2010 if certain conditions are satisfied and (ii) the amendment and restatement of our Restated Certificate of Incorporation. On November 17, 2005, we filed with the Securities and Exchange Commission a preliminary proxy statement relating to a special meeting of our stockholders at which the proposals described in the previous sentence will be made to our stockholders.

If our stockholders do not approve the issuance of the Convertible Note and Conversion Shares (a "Stockholder Approval Default"), they will cause an Event of Default under the Loan Agreement, and all amounts due under the Loan Agreement will immediately accelerate, including the loan principal plus all accrued and unpaid interest, unless MHR or its assignees elect, by notice to us, to allow such default to continue with respect to all or a part of the Loan without exercising, until further notice, any or all of their rights and remedies under the Loan Agreement. In that case, MHR or its assignees would retain all of their rights as lender thereunder, including the right to receive the various supplemental cash payments described below. At any time that MHR or its assignees elect, in their sole discretion, to exercise any or all of their rights and remedies under the Loan Agreement with respect to such default, including to receive any portion or all of the supplemental cash payments, MHR or its assignees may deliver a subsequent notice to us to elect to receive the payments described in such notice. One payment compensates MHR or its assignees for not being able to own more of our common stock. The other payment reimburses MHR or its assignees for any additional taxes they may owe for receiving cash payments instead of owning, and then selling, our common stock. The stock-based payment is the dollar value equivalent of the shares of our common stock, calculated as if MHR or its assignees had been able to convert the full loan principal amount (plus accrued and unpaid interest) into shares of our common stock at $3.78 per share and then receive any appreciation in the value of those shares of common stock until three days before MHR elects, by subsequent written notice to us, to receive a portion or all of the supplemental cash payments described in such notice. This dollar value equivalent is referred to in the Loan Agreement as the "Peak Equity Amount," and this supplemental payment is referred to in the Loan Agreement as the "Stockholder Default Balance"; both are described more fully in the Loan Agreement, as amended and Amendment No. 1 to the Loan Agreement. The tax reimbursement payment obligates us to reimburse MHR or its assignees for any additional taxes MHR or its assignees may owe as a result of receiving these cash payments instead of owning, then selling, our common stock. This tax reimbursement payment is referred to in the Loan Agreement as the "Make Whole Amount". In order to raise the funds to pay the Stockholder Default Balance and the Make Whole Amount, we will be obligated to promptly conduct a registered offering of shares of our capital stock. If the proceeds of this offering do not allow us to pay the Stockholder Default Balance and the Make Whole Amount in full, we will be obligated to conduct registered public offerings of our capital stock every 150 days for the next year and every 75 days for the subsequent four years until we fully repay MHR or its assignees. Furthermore, if the price of shares of our common stock has increased during any such 150-day period, the Peak Equity Amount will increase proportionately, and the Stockholder Default Balance will increase as well.

We expect that the special stockholders meeting will be held on December 15, 2005, although the final date will depend on the date we can mail the related proxy statement to our stockholders. The Loan Agreement also provides that an event of default shall be deemed to have occurred if we default on the payment of any obligation or indebtedness when due, any of the liens in favor of MHR created by the transaction fails to constitute a perfected lien, we suffer a bankruptcy or similar insolvency event or proceeding, we materially breach a representation or warranty or fail to observe any covenant or agreement, we suffer and do not discharge in a timely manner a final judgment for the payment of a sum in excess of a certain materiality threshold, our common stock has been delisted or trading has been suspended, we sell a substantial portion of our assets, we merge with another entity without the prior consent of MHR, or any governmental action renders us unable to honor or perform our obligations under the Loan Agreement or results in a material adverse effect on our operations. If an event of default occurs, the Loan Agreement provides for the immediate repayment of the Loan and certain additional amounts described above and as set forth in the Loan Agreement. In connection with the financing transaction, we amended MHR s existing warrants to purchase 387,374 shares of common stock to provide for additional anti-dilution protection. MHR was also granted the option to purchase warrants for up to an additional 617,211 shares of our common stock at a price per warrant equal to $0.01 per warrant for each of the first 67,084 warrants and $1.00 per warrant for each additional warrant. These warrants will have an exercise price of $4.00, subject to anti-dilution protection.

On September 23, 2005, Robert J. Levenson resigned from the Board of Directors of the Company. In connection with the MHR financing transaction, Dr. Mark Rachesky was appointed to the Board of Directors on September 23, 2005. On September 29, 2005, Michael Black and Arthur Dubroff also resigned from the Board of Directors. Mr. Dubroff held the position of Chairman of the audit committee of the Board of Directors and qualified as the audit committee financial expert, within the meaning of Item 401(h) of Regulation S-K. Due to Mr. Dubroff s resignation, these positions are currently vacant. We are working to identify a person to fill these positions and expects to do so in the time period as required by the listing requirements of the Nasdaq National Market. Also in connection with the MHR financing transaction, on October 12, 2005, Dr. Michael Weiser was appointed to the Board of Directors as a director mutually acceptable to MHR and us. Dr. Weiser is an independent director. Dr. Rachesky and Dr. Weiser have abstained and did not participate in any action or recommendation by the Board of Directors in connection with the financing transaction with MHR or of the proposals to be made to our stockholders at the special meeting in connection therewith.

On March 31, 2005, we entered into a Placement Agency Agreement (the Placement Agency Agreement) with Harris Nesbitt Corp. (the Placement Agent) pursuant to which the Placement Agent agreed to act as the exclusive placement agent, on a best efforts basis, for the issuance and sale by the Company of an aggregate of up to 4,000,000 units (the Units). Each Unit consisted of one share of our common stock and a warrant to purchase an additional 0.375 shares of common stock. The Placement Agency Agreement provided that the Placement Agent is entitled to receive 1.8% of the proceeds received by us from the sale of the Units completed on or prior to March 31, 2005. On March 31, 2005, we completed an offering and sale of 4 million Units at a price of $3.935 per Unit (the Offering), resulting in net proceeds to the Company of $15.1 million. The initial exercise price of each warrant was set at $4.00 per share. The exercise price of each warrant contains anti-dilution protection with a floor at $3.81 (as adjusted for stock splits, stock combinations and similar events). Under the terms of the warrant, we have an obligation to make a cash payment to the holders of the warrant for any gain that could have been realized if the holders exercise the warrants and we subsequently fail to deliver a certificate representing the shares to be issued upon such exercise by the third trading day after such shares have been exercised. Accordingly, the warrant has been accounted for as a liability. The fair value of the warrant was $3.9 million at the date of issuance and $4.7 million as of September 30, 2005. Pursuant to the Placement Agency Agreement, the Placement Agent received a fee of $0.3 million.

In 1996, we entered into a joint venture with Elan to develop oral heparin. In connection with the re-purchase of Elan s joint venture interest in 1999, we issued a zero coupon note (the Original Elan Note) to Elan. The Original Elan Note had an issue price of $20 million and an original issue discount at maturity of $35,048,881 for a total amount of $55,048,881 due on the maturity date of July 2, 2006. On December 27, 2004, we entered into a Security Purchase Agreement (the Security Purchase Agreement) with Elan, providing for our purchase of our indebtedness to Elan under the Original Elan Note. The value of the Original Elan Note plus accrued interest on December 27, 2004 was approximately $44 million. Pursuant to the Security Purchase Agreement, on December 27, 2004, we paid Elan $13 million and issued to Elan 600,000 shares of our common stock with a market value of approximately $2 million and, as of March 31, 2005, we completed the purchase under the Security Purchase Agreement by making a $13 million cash payment to Elan and issuing to Elan a warrant to purchase 600,000 shares of our common stock with an initial exercise price of $3.88 per share.

This transaction was accounted for as a troubled debt restructuring. The carrying amount of the debt was reduced to an amount equal to the total future cash payments, or $13 million. The fair value of the warrant issued, estimated using the Black-Scholes option pricing model, is $1.6 million. A gain of $14.7 million, calculated as the difference between the carrying value of approximately $29 million and the fair value of cash paid and warrants issued, was recognized in our condensed consolidated statement of operations for the quarter ended March 31, 2005. No interest expense was recorded during the quarter ended March 31, 2005.

On December 27, 2004, we entered into a structured secondary offering facility with Kingsbridge Capital Limited (Kingsbridge), pursuant to a Common Stock Purchase Agreement, providing for the commitment of Kingsbridge to purchase up to $20 million of our common stock until December 27, 2006. In return for the commitment, we issued to Kingsbridge a warrant to purchase 250,000 shares of our common stock with an initial exercise price of $3.811 per share. No funds have been drawn down under the Common Stock Purchase Agreement and on September 21, 2005, the agreement was terminated as a condition of closing the senior secured loan transaction with MHR. The termination of the agreement did not affect the warrants that were issued. Those warrants are still outstanding and exercisable through June 30, 2010.

On December 1, 2004 we issued a $10 million convertible note (the Novartis Note) to Novartis in connection with a new research collaboration option relating to the development of PTH 1-34. The Novartis Note bears interest at a rate of 3% prior to December 1, 2006, 5% from December 1, 2006 through December 1, 2008, and 7% from that point until maturity on December 1, 2009. We have the option to pay interest in cash on a current basis or accrue the periodic interest as an addition to the principal amount of the Novartis Note. We may convert the Novartis Note at any time prior to maturity into a number of shares of our common stock equal to the principal and accrued and unpaid interest to be converted divided by the then market price of our common stock, provided certain conditions are met, including that the number of shares issued to Novartis, when issued, does not exceed 19.9% of the total shares of our common stock outstanding, that at the time of such conversion no event of default under the Novartis Note has occurred and is continuing, and that there is either an effective shelf registration statement in effect covering the resale of the shares issued in connection with such conversion or the shares may be resold by Novartis pursuant to SEC Rule 144(k). Under the Novartis Note, an event of default shall be deemed to have occurred if we default on the payment of the principal amount of, and accrued and unpaid interest on, the Novartis Note upon maturity, we suffer a bankruptcy or similar insolvency event or proceeding, we materially breach a representation or warranty, we fail to timely cure a default in the payment of any other indebtedness in excess of a certain material threshold, or there occurs an acceleration of indebtedness in excess of that threshold, we suffer and do not discharge in a timely manner a final judgment for the payment of a sum in excess of a certain material threshold, we become entitled to terminate the registration of our securities or the filing of reports under the Securities Exchange Act of 1934, our common stock will be delisted from Nasdaq, we experience a change of control (including by, among other things, a change in the composition of a majority of our board (other than as approved by the board) in any one-year period, a merger which results in our stockholders holding shares that represent less than a majority of the voting power of the merged entity, and any other acquisition by a third party of shares that represent a majority of the voting power of the company), we sell substantially all of our assets, or we are effectively unable to honor or perform our obligations under the new research collaboration option relating to the development of PTH 1-34. Upon the occurrence of any such event of default prior to conversion, any unpaid principal and accrued interest on the Novartis Note would become immediately due and payable. If the Novartis Note is converted into our common stock, Novartis would have the right to require us to repurchase the shares of common stock within six months after an event of default under the Novartis Note, for an aggregate purchase price equal to the principal and interest that was converted, plus interest from the date of conversion, as if no conversion had occurred.

RISK FACTORS

You should carefully consider the following risk factors, as well as the other information contained in this prospectus or incorporated by reference in this prospectus, before purchasing any of our Common Stock.

We have incurred substantial losses since inception and as we expect to continue to incur development expenses for self-funded programs and partnered programs and for programs for which we are attempting to secure a partner, we are likely to require additional capital and if additional capital is not raised our ability to continue as a going concern is in substantial doubt.

Since our inception in 1986, we have generated significant losses from operations and we anticipate that we will continue to generate significant losses from operations for the foreseeable future. As of September 30, 2005, our accumulated deficit was approximately $341 million. Our net loss was $37.5 million and $44.9 million for the years ended December 31, 2004, and 2003 respectively. Net loss was $8.9 million for the nine months ended September 30, 2005. The significant decrease in net loss is a result of the $14.7 million gain on the extinguishment of the Elan note payable. Our cash outlays from operations and capital expenditures were $21.4 million for the first nine months of 2005 and $23.5 million for 2004. Our stockholders equity decreased from $67.5 million as of December 31, 2002 to a deficit of $5.9 million as of September 30, 2005. We have limited capital resources and operations to date have been funded with the proceeds from collaborative research agreements, public and private equity and debt financings and income earned on investments. These conditions raise substantial doubt about our ability to continue as a going concern. The audit report prepared by our independent registered public accounting firm relating to our consolidated financial statements for the year ended December 31, 2004 includes an explanatory paragraph expressing the substantial doubt about our ability to continue as a going concern.

As of September 30, 2005, we had cash, cash equivalents, restricted cash and investments totaling $18.3 million. We anticipate that our existing capital resources, without implementing cost reductions, raising additional capital, or obtaining substantial cash inflows from potential partners for our products, will not enable us to continue operations past March of 2006, or earlier if unforeseen events or circumstances arise that negatively affect our liquidity. These circumstances may adversely affect our ability to raise additional capital. If we fail to raise additional capital or obtain substantial cash inflows from potential or existing partners, we will be forced to cease operations. If additional capital is raised through the sale of equity or convertible debt securities, the issuance of such securities would result in dilution to our existing stockholders.

We may not be able to make the payments we owe to MHR.

On September 26, 2005, we executed a Senior Secured Loan Agreement (the Loan Agreement) with MHR. The Loan Agreement was amended on November 11, 2005 to clarify certain terms. The Loan Agreement provides for a seven year, $15 million secured loan from MHR to us at an interest rate of 11% (the Loan). The Loan is secured by a first priority lien in favor of MHR on substantially all of our assets. The proceeds from the Loan were disbursed to a restricted account and our right to have such funds disbursed to an operating account is conditioned upon the requested amounts for any period not being in excess of 103% of amounts in our budget for such period (then in effect under the terms of the Loan Agreement), and provided that we certify to MHR that no event of default has occurred under the Loan Agreement (or the Convertible Note described below, if applicable), no material adverse change has occurred and our representations and warranties under the Loan Agreement continue to be true and correct. The Loan Agreement requires us to hold a special stockholder meeting as soon as practicable, but not later than December 25, 2005, for the purpose of obtaining stockholder approval of (i) the exchange of the Loan for an 11% senior secured convertible note (the Convertible Note) with substantially the same terms as the Loan Agreement, except that the Convertible Note will be convertible, at the sole discretion of MHR or any assignee thereof, into shares of our common stock at a price per share of $3.78, interest will be payable in kind rather than in cash and we will have the right to call the Convertible Note after September 26, 2010 if certain conditions are satisfied and (ii) the amendment and restatement of our Restated Certificate of Incorporation.

If our stockholders do not approve the issuance of the Convertible Note and Conversion Shares (a "Stockholder Approval Default"), they will cause an Event of Default under the Loan Agreement, and all amounts due under the Loan Agreement will immediately accelerate, including the loan principal plus all accrued and unpaid interest, unless MHR or its assignees elect, by notice to us, to allow such default to continue with respect to all or a part of the Loan without exercising, until further notice, any or all of their rights and remedies under the Loan Agreement. In that case, MHR or its assignees would retain all of their rights as lender thereunder, including the right to receive the various supplemental cash payments described below. At any time that MHR or its assignees elect, in their sole discretion, to exercise any or all of their rights and remedies under the Loan Agreement with respect to such default, including to receive any portion or all of the supplemental cash payments, MHR or its assignees may deliver a subsequent notice to us to elect to receive the payments described in such notice. One payment compensates MHR or its assignees for not being able to own more of our common stock. The other payment reimburses MHR or its assignees for any additional taxes they may owe for receiving cash payments instead of owning, and then selling, our common stock. The stock-based payment is the dollar value equivalent of the shares of our common stock, calculated as if MHR or its assignees had been able to convert the full loan principal amount (plus accrued and unpaid interest) into shares of our common stock at $3.78 per share and then receive any appreciation in the value of those shares of common stock until three days before MHR elects, by subsequent written notice to us, to receive a portion or all of the supplemental cash payments described in such notice. This dollar value equivalent is referred to in the Loan Agreement as the "Peak Equity Amount," and this entire supplemental payment is referred to in the Loan Agreement as the "Stockholder Default Balance"; both are described more fully in the Loan Agreement, as amended, and Amendment No. 1 to the Loan Agreement. The tax reimbursement payment obligates us to reimburse MHR or its assignees for any additional taxes MHR or its assignees may owe as a result of receiving these cash payments instead of owning, then selling, our common stock. This tax reimbursement payment is referred to in the Loan Agreement as the "Make Whole Amount". In order to raise the funds to pay the Stockholder Default Balance and the Make Whole Amount, we will be obligated to promptly conduct a registered offering of shares of our capital stock. If the proceeds of this offering do not allow us to pay the Stockholder Default Balance and the Make Whole Amount in full, we will be obligated to conduct registered public offerings of our capital stock every 150 days for the next year and every 75 days for the subsequent four years until we fully repay MHR or its assignees. Furthermore, if the price of shares of our common stock has increased during any such 150-day period, the Peak Equity Amount will increase proportionately, and the Stockholder Default Balance will increase as well.

We expect that the special stockholders meeting will be held on or about December 15, 2005, although the final date will depend on the date we can mail the related proxy statement to our stockholders. The Loan Agreement also provides that an event of default shall be deemed to have occurred if we default on the payment of any obligation or indebtedness when due, any of the liens in favor of MHR created by the transaction fails to constitute a perfected lien, we suffer a bankruptcy or similar insolvency event or proceeding, we materially breach a representation or warranty or fail to observe any covenant or agreement, we suffer and do not discharge in a timely manner a final judgment for the payment of a sum in excess of a certain materiality threshold, our common stock has been delisted or trading has been suspended, we sell a substantial portion of our assets, we merge with another entity without the prior consent of MHR, or any governmental action renders us unable to honor or perform our obligations under the Loan Agreement or results in a material adverse effect on our operations. If an event of default occurs, the Loan Agreement provides for the immediate repayment of the Loan and certain additional amounts as described above and as set forth in the Loan Agreement. At such time, we may not be able to make the required payment, and if we are unable to pay the amount due under the Loan, the resulting default would have a material adverse effect on our business and on the value of our stockholders investments in our common stock.

We may not be able to make the payments we owe to Novartis.

On December 1, 2004 we issued a $10 million convertible note (the Novartis Note) to Novartis in connection with a new research collaboration option relating to the development of PTH 1-34. The Novartis Note bears interest at a rate of 3% prior to December 1, 2006, 5% from December 1, 2006 through December 1, 2008, and 7% from that point until maturity on December 1, 2009. We have the option to pay interest in cash on a current basis or accrue the periodic interest as an addition to the principal amount of the Novartis Note. In the event that interest accrues on the Novartis Note, the accretion to principal will cause future interest payments to increase. We may convert the Novartis Note at any time prior to maturity into a number of shares of our common stock equal to the principal and accrued and unpaid interest to be converted divided by the then market price of our common stock, provided certain conditions are met, including that the number of shares issued to Novartis, when issued, does not exceed 19.9% of the total shares of our common stock outstanding, that at the time of such conversion no event of default under the Novartis Note has occurred and is continuing, and that there is either an effective shelf registration

statement in effect covering the resale of the shares issued in connection with such conversion or the shares may be resold to Novartis pursuant to SEC Rule 144(k). These conditions may not be met and we may be unable to convert the Novartis Note, in which case we would be required to continue to make interest payments and the rates of such interest payments will increase over time. Under the Novartis Note, an event of default shall be deemed to have occurred if we default on the payment of the principal amount of, and accrued and unpaid interest on, the Novartis Note upon maturity, we suffer a bankruptcy or similar insolvency event or proceeding, we materially breach a representation or warranty, we fail to timely cure a default in the payment of any other indebtedness in excess of a certain material threshold, or there occurs an acceleration of indebtedness in excess of that threshold, we suffer and do not discharge in a timely manner a final judgment for the payment of a sum in excess of a certain material threshold, we become entitled to terminate the registration of our securities or the filing of reports under the Securities Exchange Act of 1934, our common stock will be delisted from Nasdaq, we experience a change of control (including by, among other things, a change in the composition of a majority of our board (other than as approved by the board) in any one-year period, a merger which results in our stockholders holding shares that represent less than a majority of the voting power of the merged entity, and any other acquisition by a third party of shares that represent a majority of the voting power of the company), we sell substantially all of our assets, or we are effectively unable to honor or perform our obligations under the new research collaboration option relating to the development of PTH 1-34. Upon the occurrence of any such event of default prior to conversion, any unpaid principal and accrued interest on the Novartis Note would become immediately due and payable. At such time, we may not be able to make the required payment, and if we are unable to pay the amount due under the Novartis Note, the resulting default would have a material adverse effect on our business and on the value of our stockholders investments in our common stock. If the Novartis Note is converted into our common stock, Novartis would have the right to require us to repurchase the shares of common stock within six months after an event of default under the Novartis Note, for an aggregate purchase price equal to the principal and interest that was converted, plus interest from the date of conversion, as if no conversion had occurred. If we are unable to make the repurchase, the resulting default would have a material adverse effect on our business and on the value of our stockholders investments in our common stock.

If we are unable to generate sufficient revenue from potential partners or raise additional capital, we will be required to curtail our development efforts, which could have a material adverse effect on our ability to realize on the commercial potential of our products.

If we fail to generate sufficient revenue or raise additional capital, we will have to undergo further restructuring and downsize our operations. Under those circumstances, our failure to restructure would have a material adverse effect on our ability to continue as a going concern. Historically, we have been able to implement cost reductions when necessary.

If our current funding is not sufficient for our operations we may be required to restructure and reduce spending, and the resultant curtailment of our development efforts could have a material adverse effect on our ability to realize the commercial potential of our products and achieve long-term profitability.

Our financial statements for the year ended December 31, 2004 emphasized the existence of substantial doubt about our ability to continue as a going concern, which may adversely affect our ability to raise additional capital.

We are highly dependent on the clinical success of our oral heparin and insulin product candidates.

Oral heparin and oral insulin are our two lead programs and are among our most advanced programs. As of June 30, 2005, we have invested $91 million and $17 million, in oral heparin and oral insulin, respectively. We believe that, based on market size, these two products, if approved, could represent our largest sources of revenue. If we fail to obtain regulatory approval for either of these products, either solely through our own efforts or through collaborations with one or more major pharmaceutical companies, our ability to fund future operations from operating revenue or issuance of additional equity is likely to be adversely affected. We are not dependent on successful culmination of clinical trials or regulatory approval of any particular one of our other product candidate programs because our investment in each such program and reward upon successful completion of each such program is substantially less significant to our long-term viability.

Oral Heparin

Heparin delivery is a highly competitive area. Other companies currently are developing spray (buccal) or alternate forms of heparin, and other anti-thrombotics have recently received European approval (e.g., AstraZeneca s EXANTA®). We are developing solid dosage forms of oral heparin and have commenced Phase III testing for the SNAC/heparin molecule combination.

We previously developed a liquid form of oral heparin and in 2000 conducted a Phase III clinical trial that was completed in early 2002. The trial did not meet its endpoint of superiority to LOVENOX®, a leading low molecular weight heparin. We believe that the trial failed to meet its endpoint of superiority possibly due in part to the poor taste of the liquid formulation. We subsequently restructured our operations, which included the discontinuation of our liquid oral heparin program and related initiatives, and a reduction of associated infrastructure. The resulting restructuring charge to earnings was approximately $1.5 million. In accordance with Statement of Financial Accounting Standards No. 144, Accounting for the Impairment or Disposal of Long-Lived Assets, in connection with the restructuring, we performed an evaluation of certain intangible and fixed assets to determine if their carrying amount exceeded their fair value. In 2003, we recorded an additional impairment charge of $5.4 million. In 2004 and 2005, we have not recorded any impairment charges.

We cannot assure you that competitive heparin products will not have an adverse effect on our heparin product development efforts or that future clinical trials related to our solid form of oral heparin will meet targeted endpoints. If future clinical trials related to oral heparin fail to meet the targeted endpoints, we likely would discontinue our oral heparin program and write off any remaining oral heparin investment.

In 1996, we formed a joint venture with Elan to develop oral forms of heparin. In July 1999, we reacquired all product, marketing and technology rights for our heparin products from Elan. In accordance with the termination agreement with Elan, we will be required to pay Elan royalties on our sales of oral heparin, subject to an annual cap of $10 million.

Oral Insulin

Insulin delivery is a highly competitive area. Other companies currently are developing buccal or aerosol (pulmonary) forms of insulin (e.g., Aventis/Pfizer/Nektar s EXUBERA®). Our oral insulin product candidate has demonstrated favorable data in early patient studies in both Type 1 and Type 2 diabetics. However, we cannot assure you that future clinical trials related to our oral insulin will meet targeted endpoints, with the result that we may fail to obtain the necessary regulatory approval for sale of oral insulin, either alone or in collaboration with a major pharmaceutical company. If such circumstances were to occur, we likely would discontinue our oral insulin program and write off any remaining oral insulin investment.

We are highly dependent upon collaborative partners to develop and commercialize compounds using our delivery agents.

A key part of our strategy is to form collaborations with pharmaceutical companies that will assist us in developing, testing, obtaining government approval for and commercializing oral forms of therapeutic macromolecules using the *e*lig*e*n® technology. We have collaborative agreements for candidates in clinical development with Novartis and Roche, and as noted below, we are in litigation with Lilly and have given Lilly notice of termination of our agreements with it.

We negotiate specific ownership rights with respect to the intellectual property developed as a result of the collaboration with each partner. While ownership rights vary from program to program, in general we retain ownership rights to developments relating to our carrier and the collaborator retains rights related to the drug product developed.

Despite our existing agreements, we cannot assure you that:

- we will be able to enter into additional collaborative arrangements to develop products utilizing our drug delivery technology;
- any existing or future collaborative arrangements will be sustainable or successful;
- the product candidates in collaborative arrangements will be further developed by partners in a timely fashion;
- any collaborative partner will not infringe upon our intellectual property position in violation of the terms of the collaboration contract; or
- milestones in collaborative agreements will be met and milestone payments will be received.

If we are unable to obtain development assistance and funds from other pharmaceutical companies to fund a portion of our product development costs and to commercialize our product candidates, we may be unable to issue equity upon favorable terms to allow us to raise sufficient capital to fund clinical development of our product candidates. Lack of funding would cause us to delay, scale back or curtail clinical development of one or more of our projects. The determination of the specific project to curtail would depend upon the relative future economic value to us of each program.

Our collaborative partners control the clinical development of the drug candidates and may terminate their efforts at will.

Novartis controls the clinical development of oral calcitonin and oral rhGH. Pending the results of our litigation with Lilly, Novartis also has an option to control the clinical development of oral PTH. Roche controls the clinical development of the small molecule compound for which they have licensed our technology. Although we influence the clinical program through participation on a Steering Committee for each product, Novartis and Roche control the decision-making for the design and timing of their respective clinical studies. As noted below, we are in litigation with Lilly and have given Lilly notice of termination of our agreements with it.

Moreover, the agreements with Novartis and Roche provide that each may terminate its programs at will for any reason and without any financial penalty or requirement to fund any further clinical studies. We cannot assure you that Novartis or Roche will continue to advance the clinical development of the drug candidates subject to collaboration.

Our collaborative partners are free to develop competing products.

Aside from provisions preventing the unauthorized use of our intellectual property by our collaborative partners, there is nothing in our collaborative agreements that prevents our partners from developing competing products. If one of our partners were to develop a competing product, our collaboration could be substantially jeopardized.

We are currently in litigation with one of our collaborative partners, and an adverse determination in that case could limit our future ability to realize on the potential value of our oral PTH 1-34 assets.

There is currently pending in the United States District Court for the Southern District of Indiana, Indianapolis Division, a lawsuit with Eli Lilly and Company. The suit results from a notice that we delivered to Lilly declaring that Lilly was in material breach of certain research and collaboration agreements entered into with Lilly with respect to the development of oral formulations of recombinant parathyroid hormone, PTH 1-34. Following receipt of the notice, Lilly filed a complaint seeking (i) a declaratory judgment declaring that Lilly is not in breach of its agreements with us concerning oral formulations of recombinant parathyroid hormone, PTH 1-34, and (ii) an order preliminarily and

permanently enjoining us from terminating those agreements. On February 12, 2004, we served Lilly with an amended counterclaim, alleging that Lilly filed certain patent applications relating to the use of our proprietary technology in combination with another drug, in violation of our agreements with Lilly, and that the activities disclosed in such applications infringe upon our patents. We are also alleging that Lilly has breached the agreements by failing to make a milestone payment of $3 million, as required upon the completion of oral PTH 1-34 product Phase I studies. Lilly has denied that the $3 million currently is due on the basis that the requisite Phase I studies have not been completed and that the patent applications that it filed relating to the use of our proprietary technology in combination with another drug is not in violation of our agreements with Lilly, and that the activities disclosed in such applications do not infringe upon our patents. On February 13, 2004, the court entered a case management plan and the parties commenced the exchange of discovery materials in March 2004. By notice dated August 23, 2004, the Company notified Lilly that in light of Lilly s ongoing, repeated and uncured violations of its PTH 1-34 license agreement, both its agreements with us were terminated. Thereafter, Lilly amended its complaint to seek a declaration that we are not entitled to terminate those agreements and also to seek declarations that Lilly has not infringed our patents. The trial has concluded and the judge is currently considering his decision. An adverse determination in this litigation concerning our claim that Lilly breached our agreements could limit our future ability to realize on the potential value of our oral PTH 1-34 assets. Although the costs of litigating this matter to its ultimate conclusion may be material, we anticipate that we will have sufficient financial resources to fund near term costs, including trial costs, and we do not anticipate any significant impact on our ability to develop our product candidates. Through September 30, 2005, we have incurred approximately $2.3 million in expenses relating to this litigation.

Although we are not currently involved in litigation with any of our other collaborative partners and have no reason to believe that such litigation will arise, it is possible that in the future this may not be the case. Were we to become involved in litigation with another of our collaborative partners, we would bear the additional expense of the litigation and we would likely suffer an adverse impact on both the program covered by the collaborative agreement and our relationship with the particular collaborative partner.

Our product candidates are in various stages of development, and we cannot be certain that any will be suitable for commercial purposes.

To be profitable, we must successfully research, develop, obtain regulatory approval for, manufacture, introduce, market and distribute our products under development, or secure a partner to provide financial and other assistance with these steps. The time necessary to achieve these goals for any individual product is long and uncertain. Before we or a potential partner can sell any of our products under development, we must demonstrate through preclinical (animal) studies and clinical (human) trials that such product is safe and effective for human use for each targeted indication. We have never successfully commercialized a drug candidate and we cannot be certain that we or our current or future partners will be able to begin, or continue, planned clinical trials for our product candidates, or if we are able, that the product candidates will prove to be safe and will produce their intended effects.

Even if safe and effective, the size of the solid dosage form, taste and frequency of dosage may impede their acceptance by patients.

A number of companies in the drug delivery, biotechnology and pharmaceutical industries have suffered significant setbacks in clinical trials, even after showing promising results in earlier studies or trials. We cannot assure you that favorable results in any preclinical study or early clinical trial will mean that favorable results will ultimately be obtained in future clinical trials. Nor can we assure you that results of limited animal and human studies are indicative of results that would be achieved in future animal studies or human clinical studies, all or some of which will be required in order to have our product candidates obtain regulatory approval. Similarly, we cannot assure you that any of our product candidates will be approved by the FDA.

For example, we initially set out to develop a liquid formulation of oral heparin. At the end of 1999, we initiated a Phase III study of our oral heparin liquid formulation. The multi-center, double-blind, double-dummy Phase III trial was referred to as the PROTECT trial (PRophylaxis with Oral SNAC/heparin against ThromboEmbolic Complications following Total hip replacement surgery).

The PROTECT trial enrolled 2,288 patients to evaluate the safety and efficacy of a solution oral heparin formulation using our *eligen*® oral drug delivery technology for the prevention of DVT in total hip replacement surgery patients (a surgical patient population that historically has had a high rate of DVT). The goal of the PROTECT trial was to demonstrate the superior efficacy and comparable safety of our oral heparin when dosed postoperatively for a 30-day regimen, as compared to injectable enoxaparin, when dosed postoperatively for a 10-day regimen. (A 10-day regimen of injectable enoxaparin, marketed by Aventis Pharma SA under the LOVENOX trademark, is the standard of care in the prevention of DVT, as determined by the American College of Chest Physicians Sixth Consensus Conference.)

The endpoint of the PROTECT trial was DVT occurrence in the 30 days following surgery, or pulmonary embolism or death. Investigators at more than 120 international sites evaluated a liquid form of heparin, consisting of the EMISPHERE delivery agent, SNAC (Sodium N-[8-(2 hydroxybenzoyl) Amino Caprylate), in combination with unfractionated heparin, when dosed orally in a 30-day regimen, compared to enoxaparin, when dosed subcutaneously (by injection) in a 10-day regimen. Total DVTs were determined by bilateral venogram, the FDA standard for measurement, measured at 30 days following surgery. A team of radiologists at Boston s Massachusetts General Hospital read all the venographies produced to determine the presence of a blood clot (thrombus).

On May 14, 2002, we announced initial results from the PROTECT study. Those initial results did not demonstrate the superiority of oral heparin, when dosed in a 30-day treatment regimen, compared to enoxaparin administered by injection in a 10-day dosing regimen in preventing DVTs.

Unless the clinical data has utility in other development programs or the safety data from the PROTECT trial is deemed useable, the termination of clinical trials for a product candidate may result in a loss of the Company s cumulative investment in the product candidate. These expenses are primarily costs of engaging clinical contract research organization and production of clinical supplies of the drug candidate.

Our future business success depends heavily upon regulatory approvals, which can be difficult to obtain for a variety of reasons, including cost.

Our preclinical studies and clinical trials, as well as the manufacturing and marketing of our product candidates, are subject to extensive, costly and rigorous regulation by various governmental authorities in the United States and other countries. The process of obtaining required approvals from the FDA and other regulatory authorities often takes many years, is expensive and can vary significantly based on the type, complexity and novelty of the product candidates. We cannot assure you that we, either independently or in collaboration with others, will meet the applicable regulatory criteria in order to receive the required approvals for manufacturing and marketing. Delays in obtaining United States or foreign approvals for our self-developed projects could result in substantial additional costs to us, and, therefore, could adversely affect our ability to compete with other companies. Additionally, delays in obtaining regulatory approvals encountered by others with whom we collaborate also could adversely affect our business and prospects. Even if regulatory approval of a product is obtained, the approval may place limitations on the intended uses of the product, and may restrict the way in which we or our partner may market the product.

The regulatory approval process presents several risks to us:

In general, preclinical tests and clinical trials can take many years, and require the expenditure of substantial resources, and the data obtained from these tests and trials can be susceptible to varying interpretation that could delay, limit or prevent regulatory approval.

Delays or rejections may be encountered during any stage of the regulatory process based upon the failure of the clinical or other data to demonstrate compliance with, or upon the failure of the product to meet, a regulatory agency s requirements for safety, efficacy and quality or, in the case of a product seeking an orphan drug indication, because another designee received approval first.

Requirements for approval may become more stringent due to changes in regulatory agency policy, or the adoption of new regulations or legislation.

The scope of any regulatory approval, when obtained, may significantly limit the indicated uses for which a product may be marketed and may impose significant limitations in the nature of warnings, precautions and contraindications that could materially affect the profitability of the drug.

Approved drugs, as well as their manufacturers, are subject to continuing and on-going review, and discovery of previously unknown problems with these products or the failure to adhere to manufacturing or quality control requirements may result in restrictions on their manufacture, sale or use or in their withdrawal from the market.

Regulatory authorities and agencies may promulgate additional regulations restricting the sale of our existing and proposed products.

Once a product receives marketing approval, the FDA may not permit us to market that product for broader or different applications, or may not grant us clearance with respect to separate product applications that represent extensions of our basic technology. In addition, the FDA may withdraw or modify existing clearances in a significant manner or promulgate additional regulations restricting the sale of our present or proposed products.

Additionally, we face the risk that our competitors may gain FDA approval for a product before us. Having a competitor reach the market before us would impede the future commercial success for our competing product because we believe that the FDA uses heightened standards of approval for products once approval has been granted to a competing product in a particular product area. We believe that this standard generally limits new approvals to only those products that meet or exceed the standards set by the previously approved product.

Our business will suffer if we cannot adequately protect our patent and proprietary rights.

Although we have patents for some of our product candidates and have applied for additional patents, there can be no assurance that patents applied for will be granted, that patents granted to or acquired by us now or in the future will be valid and enforceable and provide us with meaningful protection from competition or that we will possess the financial resources necessary to enforce any of our patents. Also, we cannot be certain that any products that we (or a licensee) develop will not infringe upon any patent or other intellectual property right of a third party.

We also rely upon trade secrets, know-how and continuing technological advances to develop and maintain our competitive position. We maintain a policy of requiring employees, scientific advisors, consultants and collaborators to execute confidentiality and invention assignment agreements upon commencement of a relationship with us. We cannot assure you that these agreements will provide meaningful protection for our trade secrets in the event of unauthorized use or disclosure of such information.

Part of our strategy involves collaborative arrangements with other pharmaceutical companies for the development of new formulations of drugs developed by others and, ultimately, the receipt of royalties on sales of the new formulations of those drugs. These drugs are generally the property of the pharmaceutical companies and may be the subject of patents or patent applications and other rights of protection owned by the pharmaceutical companies. To the extent those patents or other forms of rights expire, become invalid or otherwise ineffective, or to the extent those drugs are covered by patents or other forms of protection owned by third parties, sales of those drugs by the collaborating pharmaceutical company may be restricted, limited, enjoined, or may cease. Accordingly, the potential for royalty revenues to us may be adversely affected.

We may be at risk of having to obtain a license from third parties making proprietary improvements to our technology.

There is a possibility that third parties may make improvements or innovations to our technology in a more expeditious manner than we do. Although we are not aware of any such circumstance related to our product portfolio, should such circumstances arise, we may need to obtain a license from such third party to obtain the benefit of the improvement or innovation. Royalties payable under such a license would reduce our share of total revenue. Such a license may not be available to us at all or on commercially reasonable terms. Although we currently do not know of any circumstances related to our product portfolio which would lead us to believe that a third party has developed any improvements or innovation with respect to our technology, we cannot assure you that such circumstances will not arise in the future. We cannot reasonably determine the cost to us of the effect of being unable to obtain any such license.

We are dependent on third parties to manufacture and, in some cases, test our products.

We have a facility to manufacture a limited quantity of clinical supplies containing EMISPHERE® delivery agents. Currently, we have no manufacturing facilities for production of any therapeutic compounds under consideration as products. We have no facilities for clinical testing. The success of our self-developed programs is dependent upon securing manufacturing capabilities and contracting with clinical service providers.

The availability of manufacturers is limited by both the capacity of such manufacturers and their regulatory compliance. Among the conditions for NDA approval is the requirement that the prospective manufacturer s quality control and manufacturing procedures continually conform with the FDA s current Good Manufacturing Practice (GMP) (GMP are regulations established by the FDA that govern the manufacture, processing, packing, storage and testing of drugs intended for human use). In complying with GMP, manufacturers must devote extensive time, money and effort in the area of production and quality control and quality assurance to maintain full technical compliance. Manufacturing facilities and company records are subject to periodic inspections by the FDA to ensure compliance. If a manufacturing facility is not in substantial compliance with these requirements, regulatory enforcement action may be taken by the FDA, which may include seeking an injunction against shipment of products from the facility and recall of products previously shipped from the facility. Such actions could severely delay our ability to obtain product from that particular source.

The success of our clinical trials and our partnerships is dependent on the proposed or current partner s capacity and ability to adequately manufacture drug products to meet the proposed demand of each respective market. Any significant delay in obtaining a supply source (which could result from, for example, an FDA determination that such manufacturer does not comply with current GMP) could harm our potential for success. Additionally, if a current manufacturer were to lose its ability to meet our supply demands during a clinical trial, the trial may be delayed or may even need to be abandoned.

We may face product liability claims related to participation in clinical trials or future products.

We have product liability insurance with a policy limit of $5 million per occurrence and in the aggregate. The testing, manufacture and marketing of products for humans utilizing our drug delivery technology may expose us to potential product liability and other claims. These may be claims directly by consumers or by pharmaceutical companies or others selling our future products. We seek to structure development programs with pharmaceutical companies that would complete the development, manufacturing and marketing of the finished product in a manner that would protect us from such liability, but the indemnity undertakings for product liability claims that we secure from the pharmaceutical companies may prove to be insufficient.

We are subject to environmental, health and safety laws and regulations for which we incur costs to comply.

We use some hazardous materials in our research and development activities and are subject to environmental, health and safety laws and regulations governing the use of such materials. For example, our operations involve the controlled use of chemicals, biologicals and radioactive materials and we bear the costs of complying with the various regulations governing the use of such materials. Costs of compliance have not been material to date. While we believe we are currently in compliance with the federal, state and local laws governing the use of such materials, we cannot be certain that accidental injury or contamination will not occur. Should we be held liable or face regulatory actions regarding an accident involving personal injury or an environmental release, we potentially could incur costs in excess of our resources or insurance coverage, although, to date, we have not had to deal with any such actions. During each of 2003 and 2004, we incurred costs of approximately $200,000 in our compliance with environmental, health and safety laws and regulations.

We face rapid technological change and intense competition.

Our success depends, in part, upon maintaining a competitive position in the development of products and technologies in an evolving field in which developments are expected to continue at a rapid pace. We compete with other drug delivery, biotechnology and pharmaceutical companies, research organizations, individual scientists and non-profit organizations engaged in the development of alternative drug delivery technologies or new drug research and testing, as well as with entities developing new drugs that may be orally active. Many of these competitors have greater research and development capabilities, experience, and marketing, financial and managerial resources than we have, and, therefore, represent significant competition.

Our products, when developed and marketed, may compete with existing parenteral or other versions of the same drug, some of which are well established in the marketplace and manufactured by formidable competitors, as well as other existing drugs. For example, our oral heparin product candidate, if successful, would compete with intravenous heparin, injectable low molecular weight heparin and oral warfarin, as well as the recently approved injectable pentasaccharide and oral melagatran products. These products are marketed throughout the world by leading pharmaceutical companies such as Aventis Pharma SA, Pfizer, Inc. and Bristol Myers Squibb Company. Similarly, our salmon calcitonin product candidate, if developed and marketed, would compete with a wide array of existing osteoporosis therapies, including a nasal dosage form of salmon calcitonin, estrogen replacement therapy, selective estrogen receptor modulators, bisphosphonates and other compounds in development.

Our competitors may succeed in developing competing technologies or obtaining government approval for products before we do. Developments by others may render our product candidates, or the therapeutic macromolecules used in combination with our product candidates, noncompetitive or obsolete. For example, Nobex Corporation has an oral insulin formulation being developed and at least one competitor has notified the FDA that it is developing a competing formulation of salmon calcitonin. We cannot assure you that, if our products are marketed, they will be preferred to existing drugs or that they will be preferred to or available before other products in development.

If a competitor announces a successful clinical study involving a product that may be competitive with one of our product candidates or an approval by a regulatory agency of the marketing of a competitive product, such announcement may have a material adverse effect on our operations or future prospects resulting from reduced sales of future products that we may wish to bring to market or from an adverse impact on the price of our common stock or our ability to obtain regulatory approval for our product candidates.

We are dependent on our key personnel and if we cannot recruit and retain leaders in our research, development, manufacturing, and commercial organizations, our business will be harmed.

We are highly dependent on our executive officers. Our Chairman and CEO, Michael Goldberg, M.D., has been with Emisphere for fifteen years. We would be significantly disadvantaged if Dr. Goldberg were to leave Emisphere. The loss of other officers could have an adverse effect as well, given their specific knowledge related to our proprietary technology and personal relationships with our pharmaceutical company partners. If we are not able to retain our executive officers, our business may suffer. None of our key officers are nearing retirement age or have announced any intention to leave Emisphere. We have an employment contract with Dr. Goldberg that extends through July of 2007. We do not maintain key-man life insurance policies for any of our executive officers.

There is intense competition in the biotechnology industry for qualified scientists and managerial personnel in the development, manufacture, and commercialization of drugs. We may not be able to continue to attract and retain the qualified personnel necessary for developing our business. Additionally, because of the knowledge and experience of our scientific personnel and their specific knowledge with respect to our drug carriers the continued development of our product candidates could be adversely affected by the loss of any significant number of such personnel.

Provisions of our corporate charter documents, Delaware law and our stockholder rights plan may dissuade potential acquirors, prevent the replacement or removal of our current management and may thereby affect the price of our common stock.

Our Board of Directors has the authority to issue up to 1,000,000 shares of preferred stock and to determine the rights, preferences and privileges of those shares without any further vote or action by our stockholders. Of these 1,000,000 shares, 200,000 are currently designated Series A Junior Participating Cumulative Preferred Stock (A Preferred Stock) in connection with our stockholder rights plan, and the remaining 800,000 shares remain available for future issuance. Rights of holders of common stock may be adversely affected by the rights of the holders of any preferred stock that may be issued in the future.

We also have a stockholder rights plan, commonly referred to as a poison pill, in which Preferred Stock Purchase Rights (the Rights) have been granted at the rate of one one-hundredth of a share of A Preferred Stock at an exercise price of $80 for each share of the Company s common stock. The Rights are not exercisable or transferable apart from the common stock, until the earlier of (i) ten days following a public announcement that a person or group of affiliated or associated persons have acquired beneficial ownership of 20% or more of our outstanding common stock or (ii) ten business days (or such later date, as defined) following the commencement of, or announcement of an intention to make a tender offer or exchange offer, the consummation of which would result in the beneficial ownership by a person, or group, of 20% or more of our outstanding common stock. If we enter into consolidation, merger, or other business combinations, as defined, each Right would entitle the holder upon exercise to receive, in lieu of shares of A Preferred Stock, a number of shares of common stock of the acquiring company having a value of two times the exercise price of the Right, as defined. By potentially diluting the ownership of the acquiring company, our rights plan may dissuade prospective acquirors of our company. An amendment to the stockholder rights plan was approved in September 2005 that specifically excludes MHR from the provisions of the plan.

The A Preferred Stockholders will be entitled to a preferential cumulative quarterly dividend of the greater of $1.00 per share or 100 times the per-share dividend declared on our stock and are also entitled to a liquidation preference, thereby hindering an acquiror s ability to freely pay dividends or to liquidate the company following an acquisition. Each A Preferred Stock share will have 100 votes and will vote together with the common shares, effectively preventing an acquiror from removing existing management. The Rights contain anti-dilutive provisions, are redeemable at our option, subject to certain defined restrictions for $.01 per Right, and expire on February 23, 2006.

Additional provisions of our certificate of incorporation and by-laws could have the effect of making it more difficult for a third party to acquire a majority of our outstanding voting common stock. These include provisions that classify our Board of Directors, limit the ability of stockholders to take action by written consent, call special meetings, remove a director for cause, amend the by-laws or approve a merger with another company.

In addition, in connection with the MHR financing transaction, and after their approval by our Board of Directors, as constituted on September 26, 2005, Dr. Mark H. Rachesky was appointed to the Board of Directors by MHR (the MHR Nominee) and Dr. Michael Weiser was appointed to the Board of Directors by both the majority of our Board of Directors and MHR (the Mutual Director), as contemplated by our recently amended by-laws that also require the consent of the MHR Nominee to increase the size of the Board. Proposed amendments to our certificate of incorporation provide that the MHR Nominee and the Mutual Director may be removed only by the affirmative vote of at least 85% of the shares of common stock outstanding and entitled to vote at an election of directors. The proposed amendments to our certificate of incorporation also provide that the MHR Nominee may be replaced only by an individual designated by MHR, unless the MHR Nominee has been removed for cause, in which case the MHR Nominee may be replaced only by an individual approved by both a majority of our Board of Directors and MHR. Furthermore, the by-laws amendments and the proposed certificate of incorporation amendments provide that the rights granted to MHR by these amendments may not be amended or repealed without the unanimous vote or unanimous written consent of the Board of Directors or the affirmative vote of the holders of at least 85% of the shares of Common Stock outstanding and entitled to vote at the election of directors. The by-laws amendments and the proposed certificate of incorporation amendments, if adopted, will remain in effect as long as MHR holds at least 2% of the shares of fully diluted Common Stock. The by-laws amendments and the proposed certificate of incorporation amendments, if adopted, will have the effect of making it more difficult for a third party to gain control of our Board of Directors.

We are subject to the provisions of Section 203 of the Delaware General Corporation Law which prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. For purposes of Section 203, a business combination includes a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder, and an interested stockholder is a person who, either alone or together with affiliates and associates, owns (or within the past three years, did own) 15% or more of the corporation s voting stock.

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

The trading price for our common stock has been and is likely to continue to be highly volatile. The market prices for securities of drug delivery, biotechnology and pharmaceutical companies have historically been highly volatile. Factors that could adversely affect our stock price include:

fluctuations in our operating results; announcements of partnerships or technological collaborations,

innovations or new products by us or our competitors;

governmental regulation;

developments in patent or other proprietary rights;

public concern as to the safety of drugs developed by us or others;

the results of preclinical testing and clinical studies or trials by us, our partners or our competitors;

litigation;

general stock market and economic conditions;

number of shares available for trading (float);

inclusion in or dropping from stock indexes.

As of November 15, 2005, our 52-week high and low closing market price for our common stock was $5.92 and $2.78, respectively.

Future sales of common stock or warrants, or the prospect of future sales, may depress our stock price.

Sales of a substantial number of shares of common stock or warrants, or the perception that sales could occur, could adversely affect the market price of our common stock. As of September 30, 2005, there were outstanding options to purchase up to 4,572,523 shares of our common stock that are currently exercisable, and additional outstanding options to purchase up to 863,196 shares of common stock that are exercisable over the next several years. As of September 30, 2005, the Novartis Note is convertible into 2,876,820 shares of common stock. If the MHR Loan is exchanged for the Convertible Note upon approval by the stockholders, the Convertible Note will be convertible, at the sole discretion of MHR, into shares of common stock. At December 31, 2005, the Convertible Note would be convertible into approximately 4.1 million shares. The holders of these options and convertible securities have an opportuni ty to profit from a rise in the market price of our common stock with a resulting dilution in the interests of the other. The existence of these options may adversely affect the terms on which we may be able to obtain additional financing.

Finally, in connection with the consummation of the financing transactions with MHR, we entered into a Registration Rights Agreement with MHR (together with any of MHR s respective assignees that join the Registration Rights Agreement, the Holders). The Registration Rights Agreement obligated us to file a registration statement of which this prospectus is a part in order to register the resale of the securities of the selling stockholders referred to herein and to file an additional shelf registration statement on Form S-3 within 30 days following the date of the exchange of the Loan into the Convertible Note in order to register the resale of (a) the Convertible Note, (b) shares of our common stock issued upon conversion of the Convertible Note, and (c) any other securities that may be issued, distributed or distributable with respect thereto. The Registration Rights Agreement also obligates us to provide certain additional registration rights to the Holders, including, among others, the right to demand that we file a registration statement in order to permit the Holders to sell registrable securities held by the Holders, piggyback rights and the right to participate in any other registered offering of registrable securities by us, and the right to make an unlimited number of requests upon us to register the resale of our registrable securities held by the Holders on Form S-3.

THE TEN PINE AGREEMENT

We entered into a Consulting and Option Agreement with Ten Pine Advisors, LLC (Ten Pine), effective July 25, 2003 (the Ten Pine Agreement). Pursuant to the Ten Pine Agreement, as compensation for the services of Ten Pine, we issued to Ten Pine options (the Options) to purchase up to 50,000 shares of Common Stock. The options were issued in three tranches. The first tranche was an option to purchase up to 10,000 shares of Common Stock at an exercise price of $3.90. The second tranche was an option to purchase up to 20,000 shares of Common Stock at an exercise price of $4.875. The third tranche was an option to purchase up to 20,000 shares of Common Stock at an exercise price of $4.875. All three tranches vested immediately. Ten Pine has exercised its first option and 50% of the second option and owns 20,000 shares of Common Stock. The remainder of the second tranche and the third tranche are scheduled to expire on July 24, 2006 and July 24, 2008 respectively.

THE SELLING SHAREHOLDER

This prospectus relates to the possible resale by the selling shareholder of shares of common stock that underlie the Options issued to Ten Pine pursuant to the provisions of the Ten Pine Agreement. We are filing the registration statement of which this prospectus is a part pursuant to the provisions of the Ten Pine Agreement.

The selling shareholder may from time to time offer and sell pursuant to this prospectus any or all of the shares that it acquires upon exercise of the Options. Because the selling shareholder is not obligated to sell shares of common stock, and because the selling shareholder may also acquire or dispose of publicly traded shares of our common stock, we cannot estimate how many shares of common stock the selling shareholder will beneficially own after this offering.

The following table sets forth certain information regarding beneficial ownership of our common stock by Ten Pine as of September 30, 2005. The selling shareholder has not, within the past three years, had any position, office or other material relationship with us or any of our predecessors or affiliates, except as a result of the Ten Pine Agreement described herein.

	Shares of Common Stock Beneficially Owned Prior to the Offering (2)			Shares of Common Stock Beneficially Owned After the Offering (3)	
Selling Shareholder	Number	Percent	Number of Shares Being Offered	Number	Percent
Ten Pine Advisors, LLC (1)	50,000	(4)*	50,000	0	0%

*less than one percent

(1) The address of Ten Pine is 627 Harris Road, Bedford Hills, New York 10507.

(2) Assumes Ten Pine s exercise in full of the Options.

(3) Assumes that all of the offered shares are sold and that the selling shareholder does not acquire any other shares of our common stock.

(4) Based on the number of issued and outstanding shares of common stock as of September 30, 2005.

FORWARD-LOOKING STATEMENTS

Certain statements contained or incorporated by reference in this prospectus are forward-looking statements concerning our business, financial condition, results of operations, economic performance and financial condition. Forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and within the meaning of Section 21E of the Securities Exchange Act of 1934 are included, for example, in the discussions about:

our strategy;

new product development or product introduction;

product sales, royalties and contract revenues;

expenses and net income; and

our liquidity.

These and other forward-looking statements involve risks and uncertainties. Actual results may differ materially from those expressed or implied in those statements. Factors that could cause such differences include, but are not limited to, those discussed under the preceding section entitled Risk Factors.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of shares of our common stock by Ten Pine pursuant to this prospectus. Any proceeds received in connection with the exercise of the Options will be used for general corporate purposes, including further development of our lead clinical programs, capital expenditures and working capital requirements and the prepayment or payment at maturity of all or any portion of existing indebtedness. General corporate purposes may also include, without limitation, possible acquisitions, investments, repurchase of our capital stock and any other purposes that we may specify in any prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 50,000,000 shares of common stock, par value $.01 per share, and 1,000,000 shares of preferred stock, par value $.01 per share, of which 200,000 shares have been designated Series A Junior Participating Cumulative Preferred Stock. As of September 30, 2005, there were 23,330,706 shares of common stock outstanding and no shares of preferred stock outstanding.

Common Stock

Holders of common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, and do not have cumulative voting rights. Holders of common stock are entitled to receive ratably such dividends, if any, as may be declared by our board of directors out of funds legally available therefor, and subject to any preferential dividend rights of any then outstanding preferred stock. Upon our liquidation, dissolution or winding-up, the holders of common stock are entitled to receive ratably our net assets available after the payment of all debts and other liabilities and subject to any liquidation preference of any then outstanding preferred stock. Holders of common stock have no preemptive, subscription or conversion rights. There are no redemption or sinking fund provisions applicable to the common stock. The outstanding shares of common stock are, and the shares offered by us in this offering will be when issued and paid for, fully paid and non-assessable.

Warrants

Warrants to purchase shares of our common stock have been issued in conjunction with various financing transactions. The following table summarizes warrants outstanding as of September 30, 2005:

Related Transaction	Number of shares of common stock issuable upon exercise of the warrants (1)	Exercise period		Exercise price (1) (2)
Kingsbridge Common Stock Purchase Agreement	250,000	6/27/05	6/27/10	$ 3.81
Elan note repayment	600,000	9/30/05	9/30/10	$ 3.88
March Offering	1,500,000	3/31/05	3/31/10	$ 4.00

(1) The exercise price and the number of shares of common stock purchasable upon the exercise of the warrants are subject to adjustment upon the occurrence of specific events, including stock dividends, stock splits, and combinations of our common stock.

(2) The exercise price of the warrants is subject to adjustment upon the occurrence of certain events, including the issuance by Emisphere of common stock or common stock equivalents that have an effective price that is less than the exercise price of the warrants.

Before exercising their warrants, holders of warrants do not have any of the rights of holders of the securities purchasable upon such exercise, including, any right to receive dividends or payments upon our liquidation, dissolution or winding up or to exercise voting rights. The shares of common stock issuable upon exercise of the warrants will be, when issued in accordance with the warrants, duly and validly authorized, issued and fully paid and non-assessable. At all times that the warrants are outstanding, we will authorize and reserve at least that number of shares of common stock equal to the number of shares of common stock issuable upon exercise of all outstanding warrants.

Preferred Stock

Our board of directors has the authority, subject to certain restrictions, without further stockholder approval, to issue, at any time and from time to time, shares of preferred stock in one or more series. Each such series shall have such number of shares, designations, preferences, voting powers, qualifications, and special or relative rights or privileges as shall be determined by our board of directors, which may include, among others, dividend rights, voting rights, redemption and sinking fund provisions, liquidation preferences, conversion rights and preemptive rights, to the full extent now or hereafter permitted by the laws of the State of Delaware.

The rights of the holders of common stock will be subject to, and may be adversely affected by, the rights of holders of any preferred stock that may be issued in the future. Such rights may include voting and conversion rights which could adversely affect the holders of the common stock. Satisfaction of any dividend preferences of outstanding preferred stock would reduce the amount of funds available, if any, for the payment of dividends on common stock. Holders of preferred stock would typically be entitled to receive a preference payment.

Stockholder Rights Plan

Our board of directors has adopted a stockholder rights plan. The stockholder rights plan was adopted to give the board of directors increased power to negotiate in our best interests and to discourage appropriation of control of our Company at a price that is unfair to our stockholders. It is not intended to prevent fair offers for acquisition of control determined by our board of directors to be in our best interests and the best interests of our Company s stockholders, nor is it intended to prevent a person or group from obtaining representation on or control of our board of directors through a proxy contest, or to relieve our board of directors of its fiduciary duty concerning any proposal for our acquisition in good faith.

The stockholder rights plan involves the distribution of one right as a dividend on each outstanding share of our common stock to all holders of record on March 16, 1996, and an ongoing distribution of one right with respect to each share of our common stock issued subsequently. Each right shall entitle the holder to purchase one one-hundredth of a share of Series A Junior Participating Cumulative Preferred Stock. The rights trade in tandem with the common stock until, and become exercisable upon, the occurrence of certain triggering events, and the exercise price is based on the estimated long-term value of our common stock. The exercise of these rights becomes economically attractive upon the triggering of certain flip-in or flip-over rights which work in conjunction with the stockholder rights plan s basic provisions. The flip-in rights will permit the preferred stock s holders to purchase shares of common stock

at a discounted rate, resulting in substantial dilution of an acquiror s voting and economic interests in our company. The flip-over element of the stockholder rights plan involves certain mergers or significant asset purchases, which trigger certain rights to purchase shares of the acquiring or surviving company at a discount. The stockholder rights plan contains a permitted offer exception which allows offers determined by our board of directors to be in our best interests and the best interests of our stockholders to take place free of the diluting effects of the stockholder rights plan s mechanisms.

Our board of directors retains the right, at all times prior to acquisition of 20% of our voting common stock by an acquiror, to discontinue the stockholder rights plan through the redemption of all rights, or to amend the stockholder rights plan in any respect.

Delaware Law and Certain By-Law Provisions

Certain provisions of our by-laws are intended to strengthen our board of directors position in the event of a hostile takeover attempt. These by-law provisions have the following effects:

- they provide that only persons who are nominated in accordance with the procedures set forth in the by-laws shall be eligible for election as directors, except as may be otherwise provided in the by-laws;
- they provide that only business brought before the annual meeting by our board of directors or by a stockholder who complies with the procedures set forth in the by-laws may be transacted at an annual meeting of stockholders; and
- they establish a procedure for our board of directors to fix the record date whenever stockholder action by written consent is undertaken.

Furthermore, our Company is subject to the provisions of Section 203 of the Delaware General Corporation Law, an anti-takeover law. In general, the statute prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. For purposes of Section 203, a business combination includes a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder, and an interested stockholder is a person who, together with affiliates and associates, owns, or within three years prior, did own, 15% or more of the corporation s voting stock.

Amendments to the Company s By-Laws

In connection with the transactions contemplated by the Loan Agreement and the Investment and Exchange Agreement, on September 29, 2005, the Board of Directors approved amendments to our By-Laws, which became effective as of such date in order to provide that:

- The MHR Director may be nominated for election to the Board by MHR for so long as MHR shall continue to hold at least 2% of the shares of our outstanding Common Stock, warrants or other equity securities convertible into, or exchangeable for, any Common Stock at a conversion price or exchange rate that is equal to or less than the closing price per share of Common Stock on the trading date immediately prior to such calculation, and that the MHR Director shall, to the extent permitted by law or any applicable rule or listing standard of any applicable securities exchange or market, be a member of each committee of the Board and shall be entitled to attend a meeting of any such committee;
- MHR and the Board shall promptly select the Mutual Director, the Mutual Director shall be nominated for election to the Board and the Board shall elect the Mutual Director;
- MHR shall have the right to appoint the MHR Observer and the MHR Observer shall have the right to attend meetings of the Board and any committees thereof, solely in a non-voting capacity, and to receive all notices, written materials and other information given to directors in connection with such meetings, subject only to attorney-client privilege considerations;
- The number of directors on the Board may only be increased upon the unanimous vote or unanimous written consent of the Board;
- Any vacancy on the Board created by the resignation, removal or other discontinuation of service as a member of the Board of the MHR Director shall be filled by an individual who shall have been (i) designated by the MHR Director prior to the effectiveness of such vacancy, other than in the case of removal of the MHR Director for cause, or (ii) nominated or approved in writing by both a majority of the Board of Directors and MHR, in the case of removal of the MHR Nominee for cause;
- Any vacancy on the Board created by the resignation, removal or other discontinuation of service as a member of the Board of the Mutual Director shall only be filled by an individual who shall have been nominated or approved in writing by both a majority of the Board and MHR;

The existing removal provisions of the By-Laws be deleted in their entirety and replaced with provisions providing that any director, other than the MHR Director and the Mutual Director, may be removed, with or without cause, by the affirmative vote of the holders of a majority of the shares of common stock outstanding and entitled to vote at the election of directors and that the MHR Director and the Mutual Director, may be removed, with or without cause, by the affirmative vote of the holders of at least 85% of the shares of common stock outstanding and entitled to vote at the election of directors, provided that the stockholder vote requirement shall cease to have any force or effect after MHR shall cease to hold at least 2% of the shares of the Company s outstanding common stock, warrants or other equity securities convertible into, or exchangeable for, any Common Stock at a conversion price or exchange rate that is equal to or less than the closing price per share of Common Stock on the trading date immediately prior to such calculation;

A quorum for the transaction of business must include the MHR Director and the Mutual Director while in office instead of a mere majority of the Board;

The rights in the By-Laws appurtenant to MHR may only be altered, amended or repealed with the unanimous vote or unanimous written consent of the Board or the affirmative vote of the holders of at least 85% of the shares of common stock outstanding and entitled to vote at the election of directors, provided that the stockholder vote requirement shall cease to have any force or effect after MHR shall cease to hold at least 2% of the shares of fully diluted Common Stock; and

The Board may not adopt any resolution setting forth, or call any meeting of stockholders for the purpose of approving, any amendment to the By-Laws that would adversely affect the rights of MHR set forth therein without a vote in favor of such resolution by the MHR Director for so long as MHR continues to hold at least 2% of the shares of fully diluted Common Stock.

Transfer Agent and Registrar

Our transfer agent and registrar is Mellon Investor Services, whose offices are located at 85 Challenge Road, Ridgefield Park, New Jersey 07660, and its telephone number is 800-851-9677.

PLAN OF DISTRIBUTION

The selling shareholder may, from time to time, sell any or all of its shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling shareholder may use any one or more of the following methods when selling shares:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

short sales;

broker-dealers may agree with the selling shareholder to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling shareholder may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

The selling shareholder may also engage in short sales against the box, puts and calls and other transactions in our shares of common stock and may sell or deliver shares in connection with these trades.

Broker-dealers engaged by the selling shareholder may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling shareholder (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. Any profits on the resale of shares of common stock by a broker-dealer acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. Discounts, concessions, commissions and similar selling expenses, if any, attributable to the sale of shares will be borne by the selling stockholder. The selling shareholder may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares if liabilities are imposed on that person under the Securities Act.

The selling shareholder may from time to time pledge or grant a security interest in some or all of the shares of common stock owned by it and, if they default in the performance of its secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus after we have filed an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling shareholder to include the pledgee, transferee or other successors in interest as selling shareholder under this prospectus.

The selling shareholder also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus and may sell the shares of common stock from time to time under this prospectus after we have filed an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling shareholders to include the pledgee, transferee or other successors in interest as a selling shareholder under this prospectus.

The selling shareholder and any broker-dealers or agents that are involved in selling the shares of common stock may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares of common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act.

We are required to pay all fees and expenses incident to the registration of the shares of common stock. We have agreed to indemnify the selling shareholder against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

The selling shareholder has advised us that it has not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of its shares of common stock, nor is there an underwriter or coordinating broker acting in connection with a proposed sale of shares of common stock by any selling stockholder. If we are notified by the selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of shares of common stock, if required, we will file a supplement to this prospectus. If the selling shareholder uses this prospectus for any sale of the shares of common stock, it will be subject to the prospectus delivery requirements of the Securities Act.

LEGAL MATTERS

Certain legal matters with respect to the securities will be passed on by Brown Rudnick Berlack Israels LLP, Boston, Massachusetts.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2004 have been so incorporated in reliance on the report (which includes an explanatory paragraph relating to our ability to continue as a going concern as described in Note 1 to the financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file reports with the Securities and Exchange Commission on a regular basis that contain financial information and results of operations. You may read or copy any document that we file with the SEC at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information about the Public Reference Room by calling the SEC for more information at 1-800-SEC-0330. Our SEC filings are also available at the SEC s website at http://www.sec.gov and at our website at http://www.emisphere.com. This website address is not an active link to the registration statement of which this prospectus is a part, and any documents, links or other materials of any kind contained or referred to on such website are not part of the registration statement of which this prospectus is a part.

INCORPORATION BY REFERENCE

The SEC allows companies to incorporate by reference information filed with the SEC, 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 that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings that we will make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 and under our Commission File Number 1-10615.

1. Our Annual Report on Form 10-K and Form 10-K/A for the fiscal year ended December 31, 2004.

2. Our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2005, June 30, 2005 and September 30, 2005.

3. Our Current Reports on Form 8-K dated January 26, 2005, March 3, 2005, April 6, 2005, May 4, 2005, May 27, 2005, July 6, 2005, September 26, 2005, September 29, 2005, September 30, 2005, October 18, 2005, November 9, 2005 and November 14, 2005.

You may request a copy of these filings, at no cost, by writing or telephoning Gillian Racine at our principal executive offices at the following address:

Emisphere Technologies, Inc.
765 Old Saw Mill River Road
Tarrytown, New York 10591
(914) 593-8332

You may also request information through our website at http://www.emisphere.com. The reference to our website does not constitute incorporation by reference of the information contained at the site and you should not consider it part of this prospectus.

This prospectus is part of a registration statement we have filed with the SEC. You should rely only on the information or representations provided in this prospectus. We have authorized no one to provide you with different information. We are not making an offer of these shares of common stock in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of the document.