EMISPHERE TECHNOLOGIES INC
Form S-3
September 20, 2007

Registration No. 333-_____

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

EMISPHERE TECHNOLOGIES, INC.
(Exact name of Registrant as specified in its charter)

DELAWARE	**2834**	**13-3306985**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

765 Old Saw Mill River Road
Tarrytown, New York 10591
(914) 347-2220
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

MICHAEL V. NOVINSKI
President and Chief Executive Officer
Emisphere Technologies, Inc.
765 Old Saw Mill River Road, Tarrytown
New York 10591
(914) 347-2220
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies of Communications to:
Timothy C. Maguire, Esq.
Brown Rudnick Berlack Israels LLP
One Financial Center
Boston, MA 02111
(617) 856-8200

Approximate date of commencement of proposed sale to the public: From time to time or at one time after the effective date of this Registration Statement as determined by the Registrant.

If the only securities being registered on this Form are being offered pursuant to dividend or interest or interest investment plans, please check the following box.o

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with

dividend or interest reinvestment plans, check the following box. þ

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.o

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If this Form is a registration statement pursuant to General Instruction I. D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. o

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I. D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. o

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 as amended or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission (SEC), acting pursuant to said Section 8(a), may determine.

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities To Be Registered	Amount To Be Registered	Proposed Maximum Aggregate Offering Price Per Share(1)	Proposed Maximum Aggregate Offering Price (1)	Amount of Registration Fee
Common Stock, par value $.01 per share				
Warrants				
Total	7,000,000	$4.23	$29,610,000	$909.03

(1) In accordance with Rule 457(c), the aggregate offering price of our stock is estimated solely for calculating the registration fees due for this filing. For the initial filing of this Registration Statement, this estimate was based on the average of the high and low sales price of our stock reported by the Nasdaq Global Market on September 13, 2007, which was $4.23 per share.

THE INFORMATION IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. WE MAY NOT SELL THESE SECURITIES UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PROSPECTUS IS NOT AN OFFER TO SELL THESE SECURITIES AND WE ARE NOT SOLICITING OFFERS TO BUY THESE SECURITIES IN ANY STATE WHERE THE OFFER OR SALE IS NOT PERMITTED.

Subject to Completion, Dated September 20, 2007

Prospectus

7,000,000 shares

Common Stock
Warrants

Emisphere Technologies, Inc. may offer shares of common stock, $.01 par value per share (Common Stock) or warrants to purchase shares of Common Stock from time to time in one or more offerings. The specific terms and number of shares of Common Stock or warrants so offered will be fully described in supplements to this prospectus. Please read any prospectus supplements and this prospectus carefully before you invest. This prospectus may not be used to sell securities unless accompanied by a prospectus supplement.

Our Common Stock is traded on the Nasdaq Global Market under the symbol EMIS. On September 13, 2007, the last reported sale price for our Common Stock on the Nasdaq Global Market was $4.28 per share.

Investing in our securities involves significant risks. See Risk Factors on page 3. We may include specific risk factors in an applicable prospectus supplement under the heading Risk Factors. You should review that section of the prospectus supplement for a discussion of matters that investors in our securities should consider.

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 securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers. See Plan of Distribution. If any underwriters are involved in the sale of any securities in respect of which this prospectus is being delivered, the names of such underwriters and any applicable commissions or discounts will be set forth in a prospectus supplement. The net proceeds we expect to receive from such sale also will be set forth in a prospectus supplement.

The date of this Prospectus is _____, 2007.

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You should rely only on the information contained or incorporated by reference in this prospectus and any prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer to sell these securities in any state where the offer is not permitted. You should not assume that the information contained in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front cover of those documents.

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

ABOUT THIS PROSPECTUS

This prospectus is part of a Registration Statement on Form S-3 that we filed with the United States Securities and Exchange Commission utilizing a "shelf" registration process. Under this shelf process, we may, over the next two years, offer Common Stock or warrants described in this prospectus in one or more offerings, up to a total amount of 7,000,000 shares, either as Common Stock or as warrants to purchase shares of Common stock, in any combination thereof. Each time we use this prospectus to offer securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. Additionally, in the event there is a material change to information contained in this prospectus, we will file a post-effective amendment setting forth an explanation of such change. You should read this prospectus, any post-effective amendment, and any prospectus supplement together with additional information described below under the heading "Where You Can Find More Information."

In this prospectus, "Emisphere," "we," "us" and "our" 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 that focuses on a unique delivery of therapeutic molecules and pharmaceutical compounds using its eligen® technology. These molecules and compounds could be currently available or are in pre-clinical or clinical development. Such molecules or compounds usually cannot be delivered by the oral route of administration or the benefits of these compounds or the benefits of these compounds are limited due to poor bioavailability, slow on-set of action or variable absorption. The eligen® technology can be applied to the oral route of administration as well other delivery

pathways, such as buccal, per rectum, pulmonary, intra-vaginal or transdermal. We believe that our drug delivery technology may lead to greater patient convenience and compliance, and in some cases, improved therapies. As of August 31, 2007, we have 95 granted patents and 74 applications pending in the United States, and patents 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, osteoarthritis, osteoporosis, growth disorders, diabetes, asthma/allergies, obesity, infectious diseases and oncology. 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.

Certain Recent Developments

We anticipate that our existing capital resources will enable us to continue operations through approximately December 2007, or earlier if unforeseen events or circumstances arise that negatively affect our liquidity. If we fail to raise additional capital or obtain substantial cash inflows from existing partners prior to December 2007, we will be forced to cease operations. We are in discussions with investment bankers and others concerning our financing options.

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, 2006 includes an explanatory paragraph expressing the substantial doubt about our ability to continue as a going concern.

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 June 30, 2007, we had approximately $8.9 million in cash and investments, approximately $1.3 million in working capital, a stockholders deficit of approximately $20 million and an accumulated deficit of $408 million.

RISK FACTORS

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

If we fail to raise additional capital or receive substantial cash inflows from our partners by December of 2007 we will be forced to cease operations.

As of June 30, 2007, we had approximately $8.9 million in cash and investments, approximately $1.3 million in working capital, a stockholders deficit of approximately $20 million and an accumulated deficit of $408 million. On August 22, 2007, we completed the sale of 2 million shares of common stock and warrants to purchase 0.4 million shares of common stock resulting in a net cash inflow of approximately $7.1 million. We anticipate that we will continue to generate significant losses from operations for the foreseeable future, and that our business will require substantial additional investment that we have not yet secured. 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 related to our consolidated financial statements for the year ended December 31, 2006 includes an explanatory paragraph expressing the substantial doubt about our ability to continue as a going concern.

We anticipate that our existing capital resources will enable us to continue operations through approximately December 2007, or earlier if unforeseen events or circumstances arise that negatively affect our liquidity. If we fail to raise additional capital or obtain substantial cash inflows from existing partners prior to December 2007, we will be forced to cease operations. We are in discussions with investment bankers and others concerning our financing options.

While our plan is to raise capital when needed and/or pursue product partnering opportunities, we cannot be sure how much we will need to spend in order to develop, market and manufacture new products and technologies in the future. We expect to continue to spend substantial amounts on research and development, including amounts spent on conducting clinical trials for our product candidates. Further, we will not have sufficient resources to develop fully any new products or technologies unless we are able to raise substantial additional financing on acceptable terms or secure funds from new or existing partners. We cannot assure you that financing will be available on favorable terms or at all. 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. Our failure to raise capital when needed would adversely affect our business, financial condition and results of operations, and could force us to reduce or discontinue our operations.

We may not be able to meet the covenants detailed in the Convertible Notes with MHR Institutional Partners IIA LP, which could result in an increase in the interest rate on the Convertible Notes and/or accelerated maturity of the Convertible Notes, which we would not be able to satisfy.

On September 26, 2005, we executed a Senior Secured Loan Agreement (the "Loan Agreement") with MHR Institutional Partners IIA LP (together with its affiliates, "MHR"). The Loan Agreement, as amended, provided for a seven year, $15 million secured loan from MHR to us at an interest rate of 11% (the "Loan"). Under the Loan Agreement, MHR requested, and on May 16, 2006, we effected the exchange of the Loan for 11% senior secured convertible notes (the "Convertible Notes") with substantially the same terms as the Loan Agreement, except that the Convertible Notes are 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 the form of additional Convertible Notes rather than in cash and we have the right to call the Convertible Notes after September 26, 2010 if certain conditions are satisfied. The Convertible Notes are secured by a first priority lean in favor of MHR on substantially all of our assets.

The Convertible Notes provide for certain events of default including failure to perfect liens in favor of MHR created by the transaction, failure to observe any covenant or agreement, failure to maintain the listing and trading of our common stock, sale of a substantial portion of our assets, or merger with another entity without prior consent of MHR, or any governmental action renders us unable to honor or perform our

obligations under the Convertible Notes or results in a material adverse effect on our operations among other things. If an event of default occurs, the Convertible Notes provide for the immediate repayment of the Convertible Notes and certain additional amounts described above, at the election of the holders of the Convertible Notes. 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 Convertible Notes, the resulting default would enable MHR to foreclose on substantially all of our assets. Any of the foregoing events would have a material adverse effect on our business and on the value of our stockholders' investments in our common stock. We currently have a waiver from MHR, through August 10, 2008, for failure to perfect liens on certain intellectual property rights.

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 research collaboration option relating to the development of PTH 1-34. The Novartis Note, as amended, 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 rise. 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 Company common stock outstanding, that at the time of such conversion no event of default under the 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 Rule 144(k) under the Securities Act of 1933 (the "Securities Act"). 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) and repay the notes when due in 2009.

Under the Novartis Note, an event of default would include failure to timely cure a default in the payment of any other indebtness in excess of a certain material threshold, or there occurs an acceleration of indebtness in excess of that threshold, becoming entitled to terminate the registration of our securities or the filing of reports under the Securities Exchange Act of 1934, as amended (the Exchange Act) delisting of our common stock from NASDAQ, 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), sale of substantially all of our assets, or our inability to honor or perform our obligations under the new research collaboration option relating to the development of PTH 1-34, among other things 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. Further, if the Novartis Note has been 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.

We are highly dependent on the clinical success of our product candidates.

Our pipeline includes product candidates across all phases of clinical development. To date, we have two products in Phase III testing in collaboration with Novartis Pharma AG and its development partner, Nordic Bioscience. Both products are based on the compound, Salmon Calcitonin; one for the prevention

of osteoporosis and the other for the treatment of osteoarthritis. The osteoarthritis product has the potential to be the first disease-modifying drug that halts the progression of the illness rather than treating symptoms. The osteoarthritis program was initiated in May 2007, with the osteoporosis program initiated in February 2007. Both products use our eligen® technology to provide salmon calcitonin for the first time as a convenient oral medication.

We have three products in Phase II. The clinical program on the development of recombinant human growth hormone (rhGH) continues in collaboration with Novartis Pharma AG. We also are continuing the development of oral heparin. Discussions with the United States Food and Drug Administration (FDA) have established a pathway for the program to proceed into Phase III testing for the use of oral heparin in the prevention of deep-vein thrombosis following elective hip replacement. Currently, we are in discussion with potential partners to complete the development of oral heparin in a collaborative arrangement. Two chronic toxicology studies have been initiated. We have also resumed a clear path on the clinical development or oral insulin. An insulin/glucose clamp study with a new formulation is being planned over a three month period starting January 2008, which will provide further data and information on appropriate dosage levels. A collaborative partnership will then be investigated to complete development and determine next steps in the commercialization of this compound.

We have five products in Phase I. An Investigational New Drug Application (IND) was filed by Genta Incorporated on gallium nitrate on July 31, 2007. A Phase I program continues on an improved oral formulation of the antiviral compound acyclovir with a pharmaceutical company outside of the United States. A food-intake study for both GLP-1 and PYY will be undertaken later this year at University Hospital, Switzerland. A program involving parathyroid hormone continues on a progressive clinical development path in collaboration with Novartis Pharma AG.

We cannot assure you that our product development efforts or that future clinical trials will meet targeted endpoints or have positive outcomes.

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 eligen® technology. We have a collaborative agreement for candidates in clinical development with Novartis.

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 salmon calcitonin and oral rhGH. Novartis also has an option to control the development of oral PTH. Genta controls the clinical development of Oral Gallium. Although we influence the clinical program through participation on a Steering Committee for each product, Novartis and Genta control the decision-making for the design and timing of their respective clinical studies.

Moreover, the agreements with Novartis and Genta provide that they may terminate their 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 and Genta 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 prevent our partners from developing competing products. If one of our partners were to develop a competing product, our collaboration could be substantially jeopardized.

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 each 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.

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. 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 guidelines.
- New guidelines can have an effect on the regulatory decisions made in previous years.
- 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 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 FDA approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures continually conform with the FDA's current 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 $3 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 2004, 2005 and 2006, we incurred costs of approximately $200 thousand 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 product. 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. 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. On April 6, 2007, the Board of Directors appointed Michael V. Novinski to the position of President and Chief Executive Officer. On August 29, 2007, we hired Michael R. Garone as our Chief Financial Officer. The loss of any of our officers could have an adverse effect, 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. 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 our 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. MHR is specifically excluded 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 and are redeemable at our option, subject to certain defined restrictions for $.01 per Right. The Rights expire on April 7, 2016.

Provisions of our corporate charter documents, Delaware law and financing agreements may prevent the replacement or removal of our current management and members of our Board of Directors and may thereby affect the price of our common stock.

In connection with the MHR financing transaction, and after approval by our Board of Directors, 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. Our certificate of incorporation provides 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. Our certificate of incorporation also provides 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 amendments to the by-laws and the certificate of incorporation 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 amendments to the by-laws and the certificate of incorporation will remain in effect as long as MHR holds at least 2% of the shares of fully diluted Common Stock. The amendments to the by-laws and the certificate of incorporation will have the effect of making it more difficult for a third party to gain control of our Board of Directors.

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.

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); and
- inclusion in or dropping from stock indexes.

As of September13, 2007, our 52-week high and low closing market price for our common stock was $10.50 and $2.82, 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 June 30, 2007, there were outstanding options to purchase up to 3,550,049 shares of our common stock that are currently exercisable, and additional outstanding options to purchase up to 1,540,158 shares of common stock that are exercisable over the next several years. As of June 30, 2007, the Novartis Note is convertible into 2,607,459 shares of common stock and the MHR Convertible Notes are convertible into approximately 4,550,330 shares of our common stock. As of June 30, 2007, there were outstanding warrants to purchase 2,567,211 shares of our common stock. In connection with the sale of our stock on August 22, 2007, warrants to purchase 400,000 shares of our common stock were issued. The sale of stock resulted in an adjustment to the previously outstanding warrants, resulting in an additional 4,837 shares being available under the warrants. The holders of these options have an opportunity 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 securities may adversely affect the terms on which we may be able to obtain additional financing.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement (including any document incorporated by reference herein or therein) include forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act, that are subject to the "safe harbor" created by those sections. This forward-looking information is subject to risks and uncertainties including the factors listed under "Risk Factors," as well as elsewhere in this prospectus and any accompanying prospectus supplement. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "intends," "p "anticipates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or

comparable terminology. These statements are only predictions and may be inaccurate. Actual events or results may differ materially. In evaluating these statements, you should specifically consider various factors, including the risks outlined under Risk Factors. These factors may cause our actual results to differ materially from any forward-looking statement. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Factors that could cause actual results to differ from those reflected in forward-looking statements relating to our operations and business include:

- risks associated with our existing indebtedness;
- inability to raise future capital may cause us to cease operations;
- our ability to attract and retain key managerial and technical personnel;
- reliance on foreign sales and high customer concentration;
- dependence on collaborative partners;
- costs associated with complying with the Sarbanes-Oxley Act of 2002;
- our dependence on the clinical success of certain product candidates;
- protecting our intellectual property rights and the uncertainties of litigation;
- other risks and uncertainties, including those set forth or incorporated in this prospectus and those detailed from time to time in our filings with the SEC.

You should read this prospectus and any accompanying prospectus supplement and the documents incorporated by reference herein and therein completely and with the understanding that actual future results may be materially different from expectations. All forward-looking statements made or incorporated by reference in this prospectus and in any accompanying prospectus supplement are qualified by these cautionary statements. These forward-looking statements are made only as of the date of this prospectus, or the related prospectus supplement, as applicable, and we do not undertake any obligation, other than as may be required by law, to update or revise any forward-looking statements to reflect changes in assumptions, the occurrence of unanticipated events or changes in future operating results over time.

THE SECURITIES WE MAY OFFER

We may offer shares of Common Stock and/or warrants to purchase shares of Common Stock, in any combination thereof totaling 7,000,000 shares of Common Stock, from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

This Prospectus May Not Be Used to Consummate a Sale of Securities Unless It Is Accompanied by a Prospectus Supplement.

We may sell the securities directly to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them; and
- the net proceeds to us.

Common Stock. We may issue shares of our Common Stock from time to time. Holders of Common Stock are entitled to one vote per share on all matters submitted to a vote of stockholders. Subject to any preferences of outstanding shares of preferred stock, holders of common stock are entitled to dividends when and if declared by our board of directors.

Warrants. We may issue warrants for the purchase of Common Stock. We may issue warrants independently or together with Common Stock, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the prospectus supplements related to the series of warrants being offered, as well as the warrant agreements that contain the terms of the warrants. We will file forms of any warrants being offered through a prospectus supplement.

We will evidence each series of warrants by warrant certificates that we will issue under a separate agreement. We may enter into the warrant agreements with a warrant agent. Any warrant agent will be a bank that we select that has its principal office in the United States and a combined capital and surplus of at least $50 million. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

USE OF PROCEEDS

We currently intend to use the net proceeds from the sale of shares of common stock and/or warrants offered by this prospectus for general corporate purposes, including further development of our lead clinical programs, capital expenditures and to meet working capital needs. We will use a prospectus supplement in connection with the sale of shares of common stock and/or warrants offered by this prospectus to further specify how we intend to use any proceeds generated by such sale.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 100,000,000 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 August 31, 2007, there were 30,334,008 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 legally available funds, 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 August 31, 2007:

Related Transaction	Number of shares of common stock issuable upon exercise of the warrants (1)	Exercise period	Exercise price (1) (2)
Elan note repayment	600,000	9/30/05 – 9/30/10	$3.760
March 2005 Offering- Non MHR	967,464	3/31/05 – 3/31/10	$3.980
March 2005 Offering- MHR	387,374	3/31/05 – 3/31/10	$3.760
Warrants issued to MHR	617,211	4/10/06 – 9/26/11	$3.760
August 2007 Offering	400,000	2/22/08 – 8/21/12	$3.948

(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. The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. However,

no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a current report on Form 8-K.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the date on and after which the warrants and the related common stock will be separately transferable;
- the number of shares of common stock purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;

- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or amount of common stock issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- federal income tax consequences of holding or exercising the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the common stock purchasable upon such exercise, including the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the amount of common stock that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to 5:00 P.M. New York time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to us (or the warrant agent, if applicable) in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to us (or the warrant agent, if applicable).

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the common stock purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant

certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

The warrants and warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the Common Stock purchasable upon exercise of, its 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. The stockholder rights plan is not applicable to MHR. 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 April 7, 2006, 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 acquirer□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 acquirer, 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.

Transfer Agent and Registrar

Our transfer agent and registrar is Mellon Investor Services, whose offices are located at 480 Washington Boulevard, Jersey City, New Jersey 07310, and its telephone number is (800) 522-6645.

PLAN OF DISTRIBUTION

We may offer and sell shares of Common Stock:

- through one or more underwriters or dealers in a public offering and sale by them,
- directly to investors, or
- through agents.

We may sell shares of Common Stock from time to time in one or more transactions at a fixed price or prices, which may be changed from time to time:

- at market prices prevailing at the time of sale,
- at prices related to such prevailing market prices, or
- at negotiated prices.

We will describe the method of distribution of the shares of Common Stock in the applicable prospectus supplement. In the event there is a material change to our plan of distribution for shares offered pursuant to this prospectus, we will file a post-effective amendment to this prospectus setting forth an explanation of such change.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or purchasers of our Common Stock (as their agents in connection with the sale of shares of Common Stock). These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions or profits on resale received by the underwriters, dealers or agents may be treated as underwriting discounts and commissions. The applicable prospectus supplement will identify any such underwriter, dealer or agent, and describe any compensation received by them from us.

Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers and agents.

We may grant underwriters who participate in the distribution of shares of Common Stock an option to purchase additional shares of Common Stock to cover over-allotments, if any, in connection with the distribution.

Underwriters or agents and their associates may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

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, 2006 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 SEC 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 or the Northeast Regional Office, 3 World Financial Center, Room 4300, New York, NY 10281. 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 www.sec.gov and at our website at 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 Exchange Act and under our Commission File Number 1-10615.

1.	Our Annual Report on Form 10-K for the fiscal year ended December 31, 2006, filed with the Commission on March 6, 2007.
2.	Our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2007, filed with the Commission on May 7, 2007 and June 30, 2007, filed with the Commission on August 7, 2007.
3.	Our Current Reports on Form 8-K dated January 19, 2007, February 12, 2007, February 27, 2007 (2 reports), April 11, 2007, May 4, 2007, May 24, 2007, June 5, 2007, June 11, 2007, June 29, 2007, August 7, 2007, August 13, 2007, August 20, 2007, August 22, 2007, August 29, 2007 and September 14, 2007.

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

Emisphere Technologies, Inc.
765 Old Saw Mill River Road
Tarrytown, New York 10591
(914) 347-2220

You may also request information through our website at 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.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

An estimate (other than the SEC registration fee) of the fees and expenses of issuance and distribution (other than discounts and commissions) of the Common Stock offered hereby (all of which will be paid by us) is as follows:

SEC registration fee	$	909
Legal fees and expenses	$	25,000
Accounting fees and expenses	$	35,000
Printing costs and expenses	$	10,000
Total	$	70,909

Item 15. Indemnification of Directors and Officers.

The General Corporation Law of the State of Delaware (□DGCL□) permits us and our stockholders to limit directors□ exposure to liability for certain breaches of the directors□ fiduciary duty, either in a suit on behalf of us or in an action by our stockholders.

Our Certificate of Incorporation (the □Charter□) eliminates the liability of directors to stockholders or our Company for monetary damages arising out of the directors□ breach of their fiduciary duty of care. The Charter also authorizes us to indemnify our directors, officers, incorporators, employees and agents with respect to certain costs, expenses and amounts incurred in connection with an action, suit or proceeding by reason of the fact that such person was serving as our director, officer, incorporator, employee or agent. In addition, the Charter permits us to provide additional indemnification rights to our officers and directors and to indemnify them to the greatest extent possible under the DGCL.

We maintain a standard form of officers□ and directors□ liability insurance policy which provides coverage to our officers and directors for certain liabilities, including certain liabilities which may arise out of this Registration Statement.

Item 16. Exhibits.

The exhibits listed in the Exhibit Index as filed as part of this Registration Statement.

Exhibit Number	Description
5.1	Opinion of Brown Rudnick Berlack Israels LLP

23.1	Consent of PricewaterhouseCoopers LLP
23.2	Consent of Brown Rudnick Berlack Israels LLP (incorporated by reference to Exhibit 5.1)
24.1	Power of Attorney (included in Signature Page)

Item 17. Undertakings.

The undersigned Registrant hereby undertakes:

(1)	To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement: (i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933; (ii) to reflect in the prospectus any facts or events arising after the effective date of the Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the Registration Statement. Notwithstanding the foregoing, any increase or decrease in volume of shares of common stock offered (if the total dollar value of shares of common stock offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and (iii) to include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement; provided, however, that (i) and (ii) do not apply if the Registration Statement is on Form S-3 or Form S-8, and the information required to be included in a post-effective amendment by (i) and (ii) is contained in periodic reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the Registration Statement.
(2)	That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the shares of common stock offered therein, and the offering of such shares of common stock at that time shall be deemed to be the initial bona fide offering thereof.
(3)	To remove from registration by means of a post-effective amendment any of the shares of common stock being registered which remain unsold at the termination of the offering.
(4)	That, for the purpose of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 that is incorporated by reference in the Registration Statement shall be deemed to be a new registration statement relating to the shares of common stock offered therein,

and the offering of such shares of common stock at that time shall be deemed to be the initial bona fide offering thereof.

(5) That, for the purpose of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this Registration Statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this Registration Statement as of the time it was declared effective.

(6) That, for the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the shares of common stock offered therein, and the offering of such shares of common stock at that time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the shares of common stock being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

SIGNATURES AND POWER OF ATTORNEY

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Michael V. Novinski and Michael R. Garone, and each of them, his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments and any amendments thereto) to this Registration Statement on Form S-3 and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Tarrytown, State of New York, on September 20, 2007.

EMISPHERE TECHNOLOGIES INC

By: /s/ Michael V. Novinski
Michael V. Novinski
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated:

NAME AND SIGNATURE	TITLE	DATE
/s/ Michael V. Novinski Michael V. Novinski.	President and Chief Executive Officer (Principal Executive Officer)	September 20, 2007
/s/ Stephen K. Carter Stephen K. Carter, M.D.	Director	September 20, 2007
/s/ John D. Harkey John D. Harkey	Director	September 20, 2007

NAME AND SIGNATURE	TITLE	DATE
/s/ Howard M. Pack Howard M. Pack	Director	September 20, 2007
/s/ Mark H. Rachesky Mark H. Rachesky, M.D.	Director	September 20, 2007
/s/ Michael Weiser Michael Weiser, M.D.	Director	September 20, 2007
/s/ Michael R. Garone Michael R. Garone	Chief Financial Officer (Principal Financial and Accounting Officer)	September 20, 2007

INDEX TO EXHIBITS

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