IMARX THERAPEUTICS INC
Form 10-K
March 09, 2009

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**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**Washington, D.C. 20549**

# FORM 10-K

þ **Annual report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**
**For the fiscal year ended December 31, 2008**

o **Transition report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**
**For the Transition Period from _____ to _____**
**Commission File Number 001-33043**

**ImaRx Therapeutics, Inc.**
**(Exact Name of Registrant as Specified in Its Charter)**

| **Delaware** | **86-0974730** |
|---|---|
| **(State or Other Jurisdiction of Incorporation or Organization)** | **(I.R.S. Employer Identification No.)** |
| **12277 134th Court NE, Suite 202, Redmond, WA** | **98052** |
| **(Address of Principal Executive Offices)** | **(Zip Code)** |

**(425) 821-5501**
**(Registrant s Telephone Number, Including Area Code)**
**Securities registered pursuant to Section 12(b) of the Act:**

**None**
**Securities registered pursuant to Section 12(g) of the Act:**
**Common Stock, $0.0001 par value**
**(Title of Each Class)**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES o NO þ

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. YES o NO þ

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for at least the past 90 days. YES þ NO o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of Registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. þ

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large Accelerated Filer o Accelerated Filer o Non-accelerated filer o Smaller reporting company þ
(Do not check if a smaller reporting company)

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES o NO þ

As of February 24, 2009, there were 10,165,733 shares of the Registrant s Common Stock outstanding. As of the last day of the most recently completed second fiscal quarter (June 30, 2008), the aggregate market value of the Common Stock of the Registrant held by non-affiliates was approximately $1.4 million, based on the closing price per share of the Registrant s Common Stock on such date. This amount excludes an aggregate of 1,516,847 shares of Common Stock held by officers and directors and each person known by the Registrant to own 10% or more of the outstanding Common Stock. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, directly or indirectly, to direct or cause the direction of the management or policies of the Registrant, or that the Registrant is controlled by or under common control with such person.

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# PART I

## ITEM 1. BUSINESS

### Overview

ImaRx Therapeutics, Inc., is a development stage biopharmaceutical company whose research and development efforts have focused on the development of therapies for stroke and other vascular disorders, using our proprietary microsphere technology together with ultrasound. Our lead program, SonoLysis, involves the administration of our proprietary MRX-801 microspheres and ultrasound to break up blood clots and restore blood flow to oxygen deprived tissues. We were previously engaged in the commercialization of one drug approved by the Food and Drug Administration or FDA, urokinase. Urokinase is an FDA-approved thrombolytic, or clot-dissolving agent, indicated for the treatment of acute massive pulmonary embolism. We purchased the product from Abbott Laboratories and had been selling the product since 2006 until we sold all rights to that product to Microbix Biosystems, Inc., or Microbix, in the third quarter of 2008.

On June 11, 2008, in order to preserve capital resources, we announced a restructuring that included a significant workforce reduction in which all of our employees other than Bradford Zakes, our president and chief executive officer, and one additional employee were terminated. In furtherance of the June 2008 restructuring we discontinued substantially all research and development activity and are now exploring strategic alternatives for our clinical-stage SonoLysis program and other Company assets.

On September 23, 2008, we divested our urokinase business to Microbix. Under the terms of the agreement, Microbix acquired the remaining urokinase inventory and related assets and assumed full responsibility for ongoing commercial and regulatory activities associated with the product. Microbix paid to us an upfront payment of $2.0 million and assumed up to $0.5 million in chargeback and other liabilities for commercial product currently in the distribution channel. If the assumed chargeback and other liabilities paid by Microbix are less than $0.5 million, Microbix will issue payment to us for the difference. An additional $2.5 million payment will be made to us upon release by the FDA of three lots of urokinase that are currently subject to a May 2008 Approvable Letter. Microbix is presently working with the FDA to secure the release of the three lots of urokinase. There can be no assurances that Microbix will be successful in securing such release in a timely manner or at all. If Microbix is unable to secure the release of the three lots we will not entitled to the additional $2.5 million payment.

We are seeking strategic alternatives that would enable the continued development of our SonoLysis program and are preserving our cash resources in order to provide sufficient resources to accomplish this objective. Historically, one of our primary sources of cash has been the sale of our urokinase product. Due to the sale of the urokinase asset to Microbix, we do not currently have any significant source of cash.

### Our Development Stage Programs

*SonoLysis Program.* Our SonoLysis program involves the administration of our proprietary MRX-801 microspheres and ultrasound to break up blood clots and restore blood flow to oxygen deprived tissues. Our MRX-801 microspheres are a proprietary formulation of a lipid shell encapsulating an inert biocompatible gas. We believe the sub-micron size of our MRX-801 microspheres allows them to penetrate a blood clot, so that when ultrasound is applied their expansion and contraction, or cavitation, can break the clot into very small particles. We believe that our SonoLysis product candidate has the potential to treat ischemic stroke as well as a broad variety of other vascular disorders associated with blood clots.

Our initial therapeutic focus for our SonoLysis program has been ischemic stroke. Approximately 795,000 adults in the U.S., or one every 40 seconds, are afflicted with, and 150,000 die as a result of, some form of stroke each year. Stroke is currently the third leading cause of death, and the leading cause of disability, in the United States. Approximately 3 million Americans are currently disabled from stroke. The American Stroke Association estimates that approximately $68.9 billion was spent in the U.S. in 2009 for stroke-related medical costs and disability. The vast majority of strokes, approximately 87% according to the American Stroke Association, are ischemic in nature, meaning that they are caused by blood clots, while the remainder are the more deadly hemorrhagic strokes caused by bleeding in the brain. However, available treatment options for ischemic stroke are subject to significant therapeutic limitations. For example, the most widely used treatment for ischemic stroke is a clot-dissolving, or thrombolytic, drug that can be administered only during a narrow time window and poses a risk of bleeding, resulting in 7% or less

of ischemic stroke patients receiving such treatment. We believe that our SonoLysis program, which involves the administration of our proprietary MRX-801 microspheres and ultrasound to break up blood clots and restore blood flow to oxygen deprived tissues, has the potential to expand this narrow treatment window, thus increasing the number of stroke patients eligible to receive this therapy.

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The only FDA approved drug for the treatment of ischemic stroke is tPA. The FDA has restricted tPA s use only to patients who are able to begin treatment within three hours of onset of symptoms of ischemic stroke and who do not have certain risk factors for bleeding, such as recent surgery or taking medications that prevent clotting. To administer our SonoLysis therapy, MRX-801 microspheres are injected intravenously into the bloodstream, disperse naturally throughout the body and are carried to the site of the blood clot. Ultrasound is then administered to the site of the blood clot, and the energy from the ultrasound causes the MRX-801 microspheres to expand and contract vigorously, or cavitate. We believe this cavitation both mechanically breaks up the blood clot and helps to enhance the body s natural clot dissolving processes. The gas released by the MRX-801 microspheres is then cleared from the body by exhaling, and the lipid shell is processed like other fats in the body. Because SonoLysis therapy has the potential to be used without a thrombolytic drug and its associated risk of bleeding, we believe SonoLysis therapy may offer advantages over existing treatments for ischemic stroke, including extending the treatment window beyond three hours from onset of symptoms and broadening treatment availability to patients for whom thrombolytic drugs are contraindicated due to risk of bleeding.

In January 2008, we suspended enrollment in our Phase I/II randomized, placebo controlled clinical trial designed to evaluate the safety, tolerability and activity of escalating doses of MRX-801microspheres and ultrasound as an adjunctive therapy to tPA treatment in subjects with acute ischemic stroke. Because the safety data following the second cohort indicated that there were a greater number of intracranial hemorrhage events observed in subjects receiving treatment relative to controls in the second cohort, we concluded the study based on these findings. This effect was not observed in subjects treated in the first cohort. We have not yet conducted any clinical trials using our proprietary MRX-801 microspheres with ultrasound to treat blood clot indications without a thrombolytic drug. We estimate that if approved by the FDA over 200,000 ischemic stroke patients in the U.S. could be eligible for SonoLysis therapy.

In furtherance of the June 2008 restructuring we discontinued substantially all research and development activity and are now evaluating strategic alternatives for funding and continuation of our clinical-stage SonoLysis program and for our other Company assets.

*Additional Research Stage Opportunities*. Following our recent restructuring and significant workforce reduction, we suspended all ongoing research stage programs and are also evaluating strategic alternatives for the funding and continuation of these programs.

**Our Business Strategy**

Our goal is to become a leading provider of therapies for vascular disorders. In order to achieve this objective, our business strategy includes the following key elements:

- Obtain additional funding and/or enter into strategic partnerships to gain access to the required operating capital to continue the development of our SonoLysis program, and;
- Execute on our development plan to incrementally advance our SonoLysis program towards commercialization.

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**Industry Background**

The formation of a blood clot is a natural process by which blood thickens and coagulates into a mass of blood cells, platelets and strands of fibrin. Thrombosis occurs when a blood clot, or thrombus, begins to block a blood vessel. Formation of a clot is the body s primary mechanism for obstructing blood flow and curtailing bleeding from wounds or other injuries to blood vessels. Blood clots can be caused by a variety of factors other than injury or trauma, such as the rupture of vulnerable plaque in a vessel. Blood clots can also arise in connection with surgical and other medical procedures, such as catheter-based administration of dialysis or other treatments, which can lead to clotting around the site of an incision or within a penetrated blood vessel. An embolism occurs if all or part of a blood clot breaks away and lodges in another part of the body. When a blood clot blocks normal blood flow within the body, it can have a variety of undesirable effects, such as causing pain and swelling, ischemia or tissue damage, stroke, or even death. Over 8 million people in the U.S. are afflicted each year with complications related to blood clots. Our business is currently focused on the treatment of ischemic stroke, in which safe and rapid removal of blood clots is essential.

*Ischemic Stroke*

Approximately 795,000 adults in the U.S., or one every 40 seconds, are afflicted with, and 150,000 die as a result of, some form of stroke each year. Stroke is currently the third leading cause of death, and the leading cause of disability, in the United States. Approximately 3 million Americans are currently disabled from stroke. The American Stroke Association estimates that approximately $68.9 billion will be spent in the U.S. in 2009 for stroke related medical costs and disability.

The vast majority of strokes, approximately 87% according to the American Stroke Association, are ischemic strokes, meaning that they are caused by blood clots, while the remainder are hemorrhagic strokes, caused by bleeding in the brain, and are more deadly. However, available treatment options for ischemic stroke are subject to significant therapeutic limitations. For example, the most widely used treatment for ischemic stroke is a clot-dissolving, or thrombolytic, drug that can be administered only during a narrow time window and poses a risk of bleeding, resulting in 7% or less of ischemic stroke patients receiving such treatment.

When blood clots block arteries that supply blood to the brain, they reduce the oxygen supply to brain tissues, a condition known as cerebral ischemia which can gradually degrade the oxygen-deprived tissues and result in long-term impairment of brain functions. More than 600,000 Americans have an ischemic stroke each year. Approximately 80% of U.S. ischemic stroke patients reach an emergency room within 24 hours after the onset of stroke symptoms, according to Datamonitor; but by contrast, only about 28% of U.S. ischemic stroke patients reach an emergency room within the FDA-mandated three-hour time window for treatment with the currently approved thrombolytic drug, tPA. Due to this three-hour treatment window and other limitations, according to Datamonitor only 1.6% to 2.7% of patients with ischemic stroke in community hospitals, and only 4.1% to 6.3% in academic hospitals or specialized stroke centers, are treated with thrombolytic therapy.

***Existing Blood Clot Therapies and Their Limitations***

Various different treatments currently exist for the prevention and treatment of blood clots. Aspirin and other anti-platelets as well as heparin and other anticoagulants are commonly used to prevent or reduce the incidence of blood clots, but have no effect in eliminating such blood clots once they have formed. We focus on the treatment of blood clots once they have formed. Currently available therapeutic approaches for dissolving or otherwise eradicating blood clots before they cause serious medical consequences or death fall into two categories: clot-dissolving drugs, or thrombolytics, and mechanical devices and procedures.

*Thrombolytic Drugs*

Thrombolytic drugs dissolve blood clots by breaking up fibrin, the protein that provides the structural scaffold of blood clots. The most widely used thrombolytic drug today is a form of tissue plasminogen activator, commonly referred to as tPA. tPA is marketed in several different formulations that are approved for a variety of specific vascular disorders and is the only thrombolytic drug currently approved for the treatment of ischemic stroke.

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Thrombolytic drugs involve a variety of risks and potential side effects that can limit their usefulness:

*Risk of Bleeding* Thrombolytic drugs dissolve blood clots, including those formed naturally as a protective response to vessel injury, which can result in bleeding. The risk of bleeding increases relative to the dosage and duration of treatment and differs among the various thrombolytic drugs. Patients who are already taking other medications to prevent formation of clots, such as anticoagulants or antiplatelets, also may not be good candidates for the use of thrombolytic drugs, due to the increased difficulty of controlling bleeding. As a result, thrombolytic drugs are approved by the FDA subject to strict limitations on when, how long and in what dosages they can be administered.

*Time Window for Administration* Due to the risk of bleeding, which increases over time, tPA is only approved for administration to ischemic stroke patients within three hours after the onset of stroke symptoms. This three-hour window is considered to be one of the primary limiting factors in treating ischemic stroke. Approximately 28% of ischemic stroke patients in the U.S. recognize their symptoms and reach an emergency room within the three-hour window. However, due to other limitations, fewer than 7% of U.S. ischemic stroke patients ultimately receive treatment with a thrombolytic drug.

*Possible Immune Response* Some patients experience an immune response due to the continued administration of thrombolytic drugs. For example, thrombolytic drugs that are based on non-human biological material, such as streptokinase, which is produced using streptococcus bacteria, may stimulate such an immune reaction.

*Mechanical Devices and Procedures*

There are several mechanical means for removing or destroying blood clots. Thrombectomy, or surgical clot removal procedures are invasive and entail delays, costs and risks that accompany any major surgery. Although these procedures are less suitable for removing blood clots from the brain, there are devices approved for these cranial surgical procedures.

In addition, there are some mechanical devices that can be introduced through a catheter-based delivery system to mechanically break up a blood clot, or to ensnare and retract a clot through the vascular system and out of the body. These mechanical devices are generally not found outside of major medical centers, as they require a catheter laboratory and skilled personnel to administer the procedure. While they do not cause the same bleeding risk as thrombolytic drugs, these mechanical interventions pose some risk of damaging other tissues during treatment, as well as a risk of breaking off a piece of the clot that can itself become the cause of a stroke or embolism in some other part of the body.

**Manufacturing**

We have contracted with a third party to produce the necessary quantities of our MRX-801 microspheres for clinical research purposes.

Our contract manufacturers will be subject to unannounced inspections by the FDA and corresponding foreign and state agencies to ensure strict compliance with the FDA s current Good Manufacturing Practices, or cGMP, and other applicable governmental quality control and record-keeping regulations. We do not have control over and cannot ensure third-party manufacturers compliance with these regulations and standards. If one of our manufacturers fails to maintain compliance, the production of our product candidates could be interrupted, which could result in substantial delays, and additional costs.

**Competition**

The market for therapies to treat vascular disorders associated with blood clots is highly competitive. Numerous companies are developing competing treatments for ischemic stroke. Many of these competitors have significantly greater financial reserves than we do, and have access to greater resources. We expect that our competitors will continue to pursue the development of new or improved treatments for ischemic stroke.

Although we are unaware of any other companies that are developing microsphere technologies for therapeutic use in vascular disorders, there are two principal groups of competitors offering treatments to break up or remove blood clots: thrombolytic drug companies, and vendors of mechanical thrombectomy or similar devices.

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*Thrombolytic Drug Competitors*

The U.S. market for thrombolytic drugs is dominated by Genentech, Inc., which manufactures tPA, the most widely used thrombolytic drug. Whereas, we are aware that other thrombolytic drugs have been under development for the treatment of ischemic stroke, Genentech s tPA is currently the only thrombolytic drug that has been approved by the FDA for this indication. Other companies also offer or are developing thrombolytic drugs for treatment of blood clots associated with myocardial infarction and peripheral vascular occlusions, but since we view thrombolytic drugs as complementary to our SonoLysis therapy, we do not consider those product offerings or programs to be competitive with our current business strategy.

*Device Competitors*

One of the primary device-based treatments for ischemic stroke is the Mechanical Embolus Removal in Cerebral Ischemia retrieval system or the MERCI system, which is an intravascular catheter-based therapy marketed by Concentric Medical, Inc. This device is used to engage the clot and retract it through the catheter and out of the body. On January 7, 2008, Penumbra, Inc. announced 510(k) clearance of the Penumbra System which is also used for the revascularization of patients with acute ischemic stroke. The Penumbra System is comprised of an aspiration platform containing multiple devices that are size-matched to the specific neurovascular anatomy allowing clots to be aspirated out of intracranial vessels.

**Patents and Proprietary Rights**

Our success depends in part on our ability to develop a competitive advantage in the market through the use of microspheres and ultrasound for treatment of blood clots and vascular diseases in various parts of the body. Our ability to obtain intellectual property that protects our MRX-801 microspheres and ultrasound treatment in the presence or absence of drugs will be important to our success. Our strategy is to protect our proprietary positions by, among other things, filing U.S. and foreign patent applications related to our technology, inventions and improvements that are directed to the development of our business and our competitive advantages. Our strategy also includes developing know-how and trade secrets, and licensing technology related to bubbles and ultrasound from third parties.

The U.S. patents that we own cover certain applications related to microsphere compositions and methods of making and using such microspheres with ultrasound for the treatment of blood clots. Patents that cover our core technology expire between 2009 and 2024.

We have several pending patent claims, including allowed claims that have not yet issued, that cover additional elements of our microsphere technology. We plan to file additional patent applications on inventions that we believe are patentable and important to our business and intend to aggressively pursue and defend patent protection on our proprietary technologies.

Our ability to operate without infringing the intellectual property rights of others and to prevent others from infringing our intellectual property rights will also be important to our success. To this end, we have reviewed all patents owned by third parties of which we are aware that are related to microsphere technology and gas filled vesicles, in the presence or absence of ultrasound, and thrombolysis using gas filled vesicles, and believe that our current products do not infringe any valid claims of the third party patents that we have analyzed. There are a large number of patents directed to therapies for blood clots, and there may be other patents or pending patent applications of which we are currently unaware that may impair our ability to operate. We are currently not aware of any third parties infringing our issued claims.

When appropriate, we actively seek protection for our products, technologies, know-how and proprietary information by licensing intellectual property from third parties. We have obtained rights relating to our product candidates and future development programs from third parties as appropriate.

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**Government Regulation**

We are subject to extensive regulation by the FDA and comparable regulatory agencies in state, local and foreign jurisdictions in connection with the development, manufacture and commercialization of our product candidates.

*Categories of Regulation*

In some cases, our product candidates may fall into multiple categories and require regulatory approval in more than one category. For example, our SonoLysis therapy involves a combination of drug and device, which would require approval as a combination product before we could market either of these therapies. Our proprietary MRX-801 microspheres, which are injected into the bloodstream, have been designated as a drug by the FDA. Outside the U.S., our product candidates are also subject to regulation as drugs or medical devices, and must meet similar regulatory hurdles as in the U.S. to gain approval and reach the market.

*Drug Regulation*

The process required by the FDA before drug candidates may be marketed in the U.S. generally involves the following:

- preclinical laboratory and animal tests;
- submission and approval of an Investigational New Drug application, or IND application;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of proposed drugs for their intended use and safety, purity and potency of biologic products for their intended use;
- preapproval inspection of manufacturing facilities, company regulatory files and selected clinical investigators;
- for drugs, FDA approval of a new drug application, or NDA, or FDA approval of an NDA supplement in the case of a new indication if the product is already approved for another indication.

Prior to commencing the first human clinical trial, we must submit an IND application to the FDA. The IND application automatically becomes effective 30 days after receipt by the FDA, unless the FDA within such period raises concerns or questions about the preclinical drug testing or nonclinical safety evaluation in animals, or the design or conduct of the first proposed clinical trial. In such a case, the IND application sponsor and the FDA must resolve any outstanding concerns before the clinical trial may begin. A separate submission must be made for each successive clinical trial conducted during product development. The FDA must not object to the submission before each clinical trial may start and continue. Further, an independent Institutional Review Board, or IRB, for investigations in human subjects within each medical center in which an investigator wishes to participate in the clinical trial must review and approve the preclinical drug testing and nonclinical safety evaluation and efficacy in animals or prior human clinical trials as well as the design and goals of the proposed clinical trial before the clinical trial commences at that center. Regulatory authorities, an IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

For purposes of NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap. Moreover, the objectives of each phase may be split or combined, leading to Phase I/II and other similar trials that may be used to satisfy the requirements of otherwise separate clinical trials as follows:

*Phase I:* Phase I clinical trials are usually conducted in normal, healthy volunteers or a limited patient population to evaluate the product candidate for safety, dosage tolerance, absorption, metabolism, distribution and excretion.

*Phase II:* Phase II clinical trials are conducted in a limited patient population, the population for which the indication applies, to further identify and measure possible adverse effects or other safety risks, to determine the efficacy of the product candidate for the specific targeted disease and to determine dosage tolerance and optimal dosage. Multiple Phase II clinical trials may be conducted to obtain information prior to beginning Phase III clinical trials.

*Phase III:* When Phase II clinical trials demonstrate that a dose range of the product candidate appears to be effective and has an acceptable safety profile, Phase III clinical trials are undertaken in a larger patient population to confirm clinical efficacy and to further evaluate safety at multiple, and often internationally located, clinical trial sites.

Phase II or III studies of drugs are generally required to be listed in a public clinical trials registry, such as www.clinicaltrials.gov. The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase IV clinical studies may be made a condition to be satisfied after a drug receives

approval. The results of Phase IV clinical studies may confirm the effectiveness of a product and may provide important safety information to augment the FDA s voluntary adverse drug reaction reporting system.

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The results of product development, preclinical testing and clinical trials are submitted to the FDA as part of an NDA . The submission of an NDA must be accompanied by a user fee of several hundred thousand dollars, unless a particular waiver applies. The FDA may deny approval of an NDA if the applicable regulatory criteria are not satisfied or for any other reason, or it may require additional clinical data or an additional Phase III clinical trial. Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory agencies typically takes several years. Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the products. The FDA also closely regulates the marketing and promotion of commercialized products. A company is permitted to make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

*Medical Device Regulation*

The process required by the FDA before medical devices may be marketed in the U.S. pursuant to clearance or approval generally involves FDA review of the following:

product design, development and manufacture;

product safety, testing, labeling and storage;

preclinical testing in animals and in the laboratory; and

clinical investigations in humans.

Unless an exemption applies, each medical device distributed commercially in the U.S. requires either prior 510(k) clearance or pre-market approval, referred to as a PMA, from the FDA. The FDA classifies medical devices into one of three classes. Class I devices are subject only to general controls, such as establishment registration and device listing, labeling, medical devices reporting, and prohibitions against adulteration and misbranding. Class II medical devices require prior 510(k) clearance before they may be commercially marketed in the U.S. The FDA will clear marketing of a medical device through the 510(k) process if the FDA is satisfied that the new product has been demonstrated to have the same intended use and is substantially equivalent to another legally marketed device, including a 510(k)-cleared, or predicate, device, and otherwise meets the FDA s requirements. Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life-supporting or implantable devices, or devices deemed not substantially equivalent to a predicate device, are placed in Class III, generally requiring submission of a PMA supported by clinical trial data. Currently we have one shaker device that is a Class I device that we use to form our MRX-801 microspheres.

To obtain 510(k) clearance, a notification must be submitted to the FDA demonstrating that a proposed device is substantially equivalent to a predicate device or a device that was in commercial distribution before May 28, 1976 for which the FDA has not yet called for the submission of a PMA application. The FDA s 510(k) clearance process generally takes from three to 12 months from the date the application is submitted, but can take significantly longer. If the FDA determines that the device, or its intended use, is not substantially equivalent to a previously-cleared device or use, the device is automatically placed into Class III, requiring the submission of a PMA. Any modification to a 510(k)-cleared device that would constitute a major change in its intended use, design or manufacture, requires a new 510(k) clearance or, possibly, in connection with safety and effectiveness, a PMA.

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Clinical trials are generally required to support a PMA application and are sometimes required for 510(k) clearance. To perform a clinical trial in the U.S. for a significant risk device, prior submission of an application for an Investigational Device Exemption, or IDE to the FDA is required. An IDE amendment must also be submitted before initiating a new clinical study under an existing IDE, such as initiating a pivotal clinical trial following the conclusion of a feasibility clinical trial. The FDA responds to an IDE or an IDE amendment for a new clinical trial within 30 days. The FDA may approve the IDE or amendment, grant an approval with certain conditions, or identify deficiencies and request additional information. It is common for the FDA to require additional information before approving an IDE or amendment for a new clinical trial, and thus final FDA approval on a submission may require more than the initial 30 days. The IDE application must be supported by appropriate data, such as animal and laboratory testing results, and any available data on human clinical experience, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The animal and laboratory testing must meet the FDA s good laboratory practice requirements.

Clinical trials are subject to extensive recordkeeping and reporting requirements. Our clinical trials must be conducted under the oversight of an IRB for the relevant clinical trial sites and must comply with FDA regulations, including but not limited to those relating to good clinical practices. We, the FDA or the IRB may suspend a clinical trial at any time for various reasons, including a belief that the risks to study subjects outweigh the anticipated benefits. Even if a clinical trial is completed, the results of clinical testing may not adequately demonstrate the safety and efficacy of the device or may otherwise not be sufficient to obtain FDA approval to market the product in the U.S. Similarly, in Europe the clinical study must be approved by a local ethics committee and in some cases, including studies with high-risk devices, by the ministry of health in the applicable country.

Once a device is in commercial distribution, we or our agents are subject to ongoing regulatory compliance including Quality System Regulation and cGMP compliance, recordkeeping, adverse experience reporting, and conformity of promotion and advertising materials to the approved instructions for use.

*Regulatory Enforcement*

Failure to comply with applicable regulatory requirements can result in enforcement action by the FDA or state authorities, which may include any of the following sanctions:

warning letters, fines, injunctions, consent decrees and civil penalties;

product recalls or market withdrawals;

customer notifications, repair, replacement, refunds, recall or seizure of our products;

operating restrictions, partial suspension or total shutdown of production;

refusal to grant new regulatory approvals;

withdrawing NDAs, 510(k) clearance or PMA that have already been granted; and

criminal prosecution.

**Employees**

We have two full-time employees who are engaged in executive, administrative, accounting and business development functions. None of our employees is covered by a collective bargaining agreement.

**Available Information**

Our Internet website address is www.imarx.com. We provide free access to various reports that we file with, or furnish to, the United States Securities and Exchange Commission, or SEC, through our website, as soon as reasonably practicable after they have been filed or furnished. These reports include, but are not limited to, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and any amendments to those reports. Our SEC reports can be accessed through the investor relations section of our website, or through www.sec.gov. Also available on our website are printable versions of ImaRx s Code of Conduct and charters of the Audit, Compensation, and Nominating and Governance Committees of our Board of Directors. Information on our website does not constitute part of this annual report on Form 10-K or any other report we file or furnish with the

SEC.

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## ITEM 1A. RISK FACTORS

**The following important factors, among others, could cause our actual operating results to differ materially from those indicated or suggested by forward-looking statements made in this Annual Report on Form 10-K or presented elsewhere by management from time to time.**

### Risks Related to Our Business and Industry

***Unless we are able to generate sufficient product or other revenue, we will continue to incur losses from operations and may never achieve or maintain profitability.***

We have a history of net losses and negative cash flow from operations since inception. As of December 31, 2008, we had an accumulated deficit of $91.3 million. We have incurred losses in each year since our inception. Our net losses applicable to common stockholders for the fiscal years ended December 31, 2008 and 2007 were $10.1 million and $18.6 million, respectively. We currently do not have sufficient cash resources to further product development activities. However, if and when we are successful in obtaining such resources, we expect our product development expenses to increase in connection with our ongoing and future product development initiatives. Because of the numerous risks and uncertainties associated with developing new medical drugs and devices, we are unable to predict the extent of any future losses or when we will become profitable, if ever.

***Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern.***

We have received an audit report from our independent registered accounting firm containing an explanatory paragraph stating that our historical recurring losses from operations which has resulted in an accumulated deficit of $91.3 million at December 31, 2008 raises substantial doubt about our ability to continue as a going concern.

***We will need additional capital to fund our present operations beyond the third quarter 2009. If we are unable to identify or consummate an attractive strategic transaction for our SonoLysis program or our other assets in a timely manner we may be forced to delay, reduce or eliminate these activities and we may be unable to timely pay our debts.***

We do not currently have sufficient cash resources to fund any product development activities. Our current activities are directed toward securing an attractive strategic transaction for our SonoLysis program and our other assets. We believe that our cash and cash equivalents will be sufficient to fund these activities and other demands and commitments into the third quarter 2009. Our funding requirements will, however, depend on numerous factors, including:

- whether Microbix is successful in obtaining lot release from the FDA with respect to the three lots currently subject to an FDA Approvable Letter:
- the timing and amount of revenue from a strategic transaction for our clinical-stage SonoLysis program and our other assets;
- personnel, facilities and equipment requirements; and
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims and other patent-related costs, including litigation costs, if any, and the result of any such litigation.

We cannot be certain that we will generate any additional funding. We may be forced to accept terms on a strategic transaction that are highly dilutive or otherwise disadvantageous to our existing stockholders. If we are unable to secure adequate financing, we could be required to liquidate the remaining assets.

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***Our competitors generally are larger than we are, have greater financial resources available to them than we do and may have a superior ability to develop and commercialize competitive products. In addition, if our competitors have products that are approved in advance of ours, marketed more effectively or demonstrated to be safer or more effective than ours, our commercial opportunity will be reduced or eliminated and our business will be harmed.***

Our industry sector is intensely competitive, and we expect competition to continue to increase. Many of our actual or potential competitors have substantially longer operating histories and greater financial, research and development and marketing capabilities than we do. Many of them also have substantially greater experience than we have in undertaking preclinical studies and clinical trials, obtaining regulatory approvals and manufacturing and distributing products. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical companies. In addition, academic institutions, government agencies and other public and private research organizations also conduct research, seek patent protection and establish collaborative arrangements for product development and marketing. We may not be able to develop products that are more effective or achieve greater market acceptance than our competitors products. Any company that brings competitive products to market before us may achieve a significant competitive advantage.

We believe that the primary competitive factors in the market for treatments of vascular disorders include safety and efficacy, access to and acceptance by leading physicians, cost-effectiveness, physician relationships and sales and marketing capabilities. We may be unable to compete successfully on the basis of any one or more of these factors, which could have a material adverse effect on our business, financial condition and results of operations.

***If we are unable to develop, manufacture and commercialize our product candidate, we may not generate sufficient revenue to continue our business.***

The process to develop, obtain regulatory approval for and commercialize potential drug candidates is long, complex and costly. Our proprietary SonoLysis microsphere technology has not been used in clinical trials other than our concluded Phase I/II clinical trial. As a result, our business in the near term is substantially dependent upon our ability to complete development, obtain regulatory approval for and commercialize our SonoLysis product candidate in a timely manner. If we are unable to commercialize or license our SonoLysis product candidates, we may not be able to earn sufficient revenue to continue our business.

***We do not plan to manufacture any of our product candidates and will depend on commercial contract manufacturers to manufacture our products.***

We do not have our own manufacturing facilities, have no experience in large-scale product manufacturing, and do not intend to develop such facilities or capabilities. Our ability to conduct clinical trials and commercialize our product candidates will depend, in part, on our ability to manufacture our products through contract manufacturers. For all of our product candidates, we or our contract manufacturers will need to have sufficient production and processing capacity to support human clinical trials, and if those clinical trials are successful and regulatory approvals are obtained, to produce products in commercial quantities. Delays in providing or increasing production or processing capacity could result in additional expense or delays in our clinical trials, regulatory submissions and commercialization of our products. In addition, we will be dependent on such contract manufacturers to adhere to the FDA s current Good Manufacturing Practices, or cGMP, and other regulatory requirements.

Establishing contract manufacturing is costly and time-consuming and we cannot be certain that we will be able to engage contract manufacturers who can meet our quantity and quality requirements in a timely manner and at competitive costs. The manufacturing processes for our product candidates have not yet been tested at commercial levels, and it may not be possible to manufacture such materials in a cost-effective manner. Further, there is no guarantee that the components of our proposed drug product candidates will be available to our manufacturers when needed on terms acceptable to us.

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***Our product candidates may never achieve market acceptance.***

We cannot be certain that our products will achieve any degree of market acceptance among physicians and other health care providers and payers, even if necessary regulatory approvals are obtained. We believe that recommendations by physicians and other health care providers and payers will be essential for market acceptance of our products, and we cannot be certain we will ever receive any positive recommendations or reimbursement. Recently, the labels of certain microspheres currently being commercialized as contrast agents for use in echocardiography were revised by the FDA to include warnings with respect to certain serious cardiopulmonary reactions, including fatalities observed when the bubbles were administered during echocardiography. One of the microspheres marketed under the brand name Definity® is similar in composition to our MRX-801 microsphere. As a result, our MRX-801 microsphere, if approved, may receive a similar warning that could negatively impact use of our product by physicians and may require us to conduct additional clinical tests, which would increase our development costs and may delay commercialization of our product. Physicians will not recommend our products unless they conclude, based upon clinical data and other factors, that our products are safe and effective. We are unable to predict whether any of our product candidates will ever achieve market acceptance, either in the U.S. or internationally. A number of factors may limit the market acceptance of our products, including:

- the timing and scope of regulatory approvals of our products and market entry compared to competitive products;
- the safety and efficacy of our products, including any inconveniences in administration, as compared to alternative treatments;
- the rate of adoption of our products by hospitals, doctors and nurses and acceptance by the health care community;
- the product labeling and marketing claims permitted or required by regulatory agencies for each of our products;
- the competitive features of our products, including price, as compared to competitive products;
- the availability of sufficient third party coverage or reimbursement for our products;
- the extent and success of our sales and marketing efforts; and
- possible unfavorable publicity concerning our products or any similar products.

If our products are not commercialized, our business will be materially harmed.

***Technological change and innovation in our market sector may cause our products to become obsolete shortly after or even before such products reach the market.***

New products and technological development in the pharmaceutical and medical device industries may adversely affect our ability to complete required regulatory requirements and introduce our product candidates into the market or may render our products obsolete. The markets into which we plan to introduce our products are characterized by constant and sometimes rapid technological change, new and improved product introductions, changes in regulatory requirements, and evolving industry standards. Our ability to execute our business plan will depend to a substantial extent on our ability to identify new market trends and develop, introduce and support our candidate products on a timely basis. If we fail to develop and commercialize our product candidates on a timely basis, we may be unable to compete effectively. If we eventually succeed at obtaining regulatory approval for commercial sale of our product candidate, competitive developments may have diminished our product opportunities, which would have an adverse impact on our business prospects and financial condition.

***We intend to rely heavily on third parties to implement critical aspects of our business strategy, and our failure to enter into and maintain these relationships on acceptable business terms, or at all, would materially adversely affect our business.***

We intend to rely on third parties for certain critical aspects of our business, including:

- manufacturing of our MRX-801 and other proprietary microspheres;
- conducting clinical trials;

conducting preclinical studies;

preparing, submitting and maintaining regulatory records sufficient to meet the requirements of the FDA; and

customer logistics and distribution of our products.

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We do not currently have agreements in place for all of these services. Although we use a third party manufacturer to produce MRX-801 microspheres for our research purposes on a purchase order basis, that third party may not have the capacity to produce the volume of MRX-801 microspheres necessary for commercial sales. To the extent that we are unable to maintain the relationships we have in place or to enter into any one or more of the additional relationships necessary to conduct our business on commercially reasonable terms, or at all, or to eliminate the need for any such relationship by establishing our own capabilities in a particular functional area in a timely manner, we could experience significant delays or cost increases that could have a material adverse effect on our ability to develop, manufacture and commercialize our product and product candidates.

***We rely on third party products, technology and intellectual property, which could negatively affect our ability to sell our MRX-801 microspheres or other products commercially or could adversely affect our ability to derive revenue from such products.***

Our SonoLysis program may require the use of multiple proprietary technologies, including commercially available ultrasound devices and patented technologies. Manufacturing our products or customizing related ultrasound devices may also require licensing technologies and intellectual property from third parties. Obtaining and maintaining licenses for these technologies may require us to make royalty payments or other payments to several third parties, potentially reducing our revenue or making the cost of our products commercially prohibitive. We cannot be certain that we will be able to establish any or all of the partnering relationships and technology licenses that may be necessary for the pursuit of our business strategy, or, even if such relationships can be established, that they will be on terms favorable to us or that they can be managed in a way that will assist us in executing our business plan.

***We have only two full-time employees and consulting relationships with certain key consultants to provide necessary services. We may not have sufficient personnel to effectively identify or consummate an attractive strategic transaction for our clinical-stage SonoLysis program and other Company assets in a timely manner, or at all.***

Our success depends substantially on the services of our two employees and key consultants. The loss of the services of one or more of these persons could have a material adverse effect on our business. Each of these persons may terminate his or her relationship with us without notice and without cause or good reason. Our ability to identify or consummate an attractive strategic transaction for our clinical-stage SonoLysis program and other Company assets is substantially dependent on these persons and without them we cannot be certain that we will be able to do accomplish our business objectives.

***We may be unable to manage our company s growth effectively.***

If we engage in a pivotal clinical trial or commercialization efforts in the future, our business will undergo significant growth. For example, we may have to expand existing operations in order to conduct a pivotal trial and additional clinical trials, increase our contract manufacturing capabilities, hire and train new personnel to handle the marketing and sales of our products, assist in obtaining reimbursement for the use of our products, and create and develop new applications for our technology. Such growth may place significant strain on our management, financial and operational resources. Successful growth is also dependent upon our ability to implement appropriate financial and management controls, systems, and procedures. Our ability to effectively manage growth depends on our success in attracting and retaining highly qualified personnel, for which the competition may be intense. If we fail to manage these challenges effectively, our business could be harmed.

***We depend on patents and other proprietary rights, some of which are uncertain and unproven. Further, our patent portfolio and other intellectual property rights are expensive to maintain, protect against infringement claims by third parties, and enforce against third party infringements, and are subject to potential adverse claims.***

Because we are developing product candidates that rely on advanced and innovative technologies, our ability to execute our business plan will depend in large part on our ability to obtain and effectively use patents and licensed patent rights, preserve trade secrets and operate without infringing upon the proprietary rights of others.

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The patent position of pharmaceutical, medical device and biotechnology companies in general is highly uncertain and involves complex legal and factual questions. Effective intellectual property protection may also be unavailable or limited in some foreign countries. We have not pursued foreign patent protection in all jurisdictions or for all of our patentable intellectual property. As a result, our patent protection for our intellectual property will likely be less comprehensive if and when we commence international sales.

There are also companies that are currently commercializing FDA approved microspheres-based products for diagnostic uses. These companies may promote these products for off-label uses which may directly compete with our products when and if approved. Additionally, physicians may prescribe the use of such products for off-label indications which could have the impact of reducing our revenues for our product candidates when and if approved.

In the U.S. and internationally, enforcing intellectual property rights against infringing parties is often costly. Pending patent applications may not issue as patents and may not issue in all countries in which we develop, manufacture or sell our products or in countries where others develop, manufacture and sell products using our technologies. Patents issued to us may be challenged and subsequently narrowed, invalidated or circumvented. In February 2005, a third party filed an opposition claim to one of our patents in Europe that relates to targeted bubbles for therapeutic and diagnostic use. The third party agreed to voluntarily dismiss and terminate this claim, but other such conflicts could occur and could limit the scope of the patents that we may be able to obtain or may result in the denial of our patent applications. If a third party were to obtain intellectual property protection for any of the technologies upon which our business strategy is based, we could be required to challenge such protections, terminate or modify our programs that rely on such technologies or obtain licenses for use of these technologies. For example, in July 2003 we received a notice from a third party who owns a patent relating to the administration of ultrasound to break up blood clots indicating that we may need a license to its patent if we intend to administer our therapies according to its patented method. Although we do not intend to administer our therapies according to the third party s patented method, other similar third party patents, if valid, could require us to seek a license that may not be available on terms acceptable to us or at all, could impose limitations on how we administer our therapies, and may require us to adopt restrictions or requirements as to the manner of administration of our products that we might not otherwise adopt to avoid infringing patents of others. Moreover, we may not have the financial resources to protect our patent and other intellectual property rights and, in that event, our patents may not afford meaningful protection for our technologies or product candidates, which would materially adversely affect our ability to develop and market our product candidates and to generate licensing revenue from our patent portfolio.

Additional risks related to our patent rights and other proprietary rights include:

- challenge, invalidation, circumvention or expiration of issued patents already owned by or licensed to us;
- claims by our consultants, key employees or other third parties that our products or technologies are the result of technological advances independently developed by them and, therefore, not owned by us;
- our failure to pay product development costs, license fees, royalties, milestone payments or other compensation required under our technology license and technology transfer agreements, and the subsequent termination of those agreements;
- failure by our licensors or licensees to comply with the terms of our license agreements;
- misrepresentation by technology owners of the extent to which they have rights to the technologies that we purport to acquire or license from them; and
- loss of rights that we have licensed due to our failure or decision not to fund further research or failure to achieve required development or commercialization milestones or otherwise comply with our obligations under the license and technology transfer agreements.

If any of these events occurs, our business may be harmed.

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***Other companies may claim that we infringe their patents or trade secrets, which could subject us to substantial damages.***

A number of third parties, including certain of our competitors, have developed technologies, filed patent applications or obtained patents on technologies and compositions that are related to aspects of our business, including thrombolytic drug therapy, microspheres and ultrasound. Such third parties may sue us for infringing their patents. If we face an infringement action, defending against such an action could require substantial resources that may not be available to us. In the event of a successful claim of infringement against us, we may be required to:

pay substantial damages;

stop using infringing technologies and methods;

stop certain research and development efforts;

develop non-infringing products or methods; and

obtain one or more licenses from third parties.

Any claims of infringement could cause us to incur substantial costs and could divert management s attention away from our business in defending against the claim, even if the claim is invalid. A party making a claim could secure a judgment that requires us to pay substantial damages. A claim of infringement could also be used by our competitors to delay market introduction or acceptance of our products. If we are sued for infringement, we could encounter substantial delays in development, manufacture and commercialization of our product candidates. Any litigation, whether to enforce our patent rights or to defend against allegations that we infringe third party rights, will be costly and time consuming and will likely distract management from other important tasks.

***Our rights to develop and commercialize our SonoLysis product candidate is subject to the terms and conditions of licenses or sublicenses granted to us by third parties, including other pharmaceutical companies, that contain restrictions that may limit our ability to capitalize on this product.***

Our SonoLysis therapy product candidate is based in part on patents and other intellectual property that we license or sublicense from third parties. Our rights to develop and commercialize this product candidate using intellectual property licensed from UNEMED Corporation may terminate, in whole or in part, if we fail to pay royalties to third party licensors, or if we fail to comply with certain restrictions regarding our development activities. In the event of an early termination of any such license or sublicense agreement, rights licensed and developed by us under such agreements may be extinguished, and our rights to the licensed technology may revert back to the licensor. Any termination or reversion of our rights to develop or commercialize any such product candidate may have a material adverse effect on our business.

We are party to an agreement with Bristol-Myers Squibb that restricts us from using our bubble technology for non-targeted diagnostic imaging applications. Bristol-Myers Squibb also has a right of first negotiation should we wish to license to a third party any of our future products or technology related to the use of bubbles for targeted imaging of blood clots, or breaking up blood clots with ultrasound and bubbles. Bristol-Myers Squibb has waived its rights under this agreement with respect to our current generation of MRX-801 microspheres that we are developing for breaking up blood clots, as well as a new generation of MRX-802 microspheres that we are developing for breaking up blood clots that include targeting mechanisms to cause the bubbles to attach to blood clots. This right of first negotiation for future technology we may develop in these applications could adversely impact our ability to attract a partner or acquirer for SonoLysis therapy.

In addition, we have been awarded various government funding grants and contracts from The National Institutes of Health and other government agencies. These grants include provisions that provide the U.S. government with the right to use the technologies developed under such grants for certain uses, under certain circumstances. If the government were to exercise its rights, our ability to commercialize such technology would likely be impaired.

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***We could be exposed to significant product liability claims, which could be time consuming and costly to defend, divert management attention and adversely impact our ability to obtain and maintain insurance coverage. The expense and potential unavailability of insurance coverage for our company or our customers could adversely affect our ability to sell our products, which would negatively impact our business.***

We face a risk of product liability exposure related to the testing of our product candidates in clinical trials and will face even greater risks upon any commercialization by us of our product candidates. Thrombolytic drugs are known to involve certain medical hazards, such as risks of bleeding or immune reactions. Our product candidates may also involve presently unknown medical risks of equal or even greater severity. Product liability claims or other claims related to our products, or their off-label use, regardless of their merits or outcomes, could harm our reputation in the industry, and reduce our product sales. Additionally, any lawsuits or product liability claims against us may divert our management from pursuing our business strategy and may be costly to defend. Further, if we are held liable in any of these lawsuits, we may incur substantial liabilities and may be forced to limit or forego further commercialization of one or more of our products. A product liability related claim or recall could be materially detrimental to our business. Our current product liability insurance, which provides us with $10 million of coverage in the aggregate, may be insufficient. We may not be able to obtain or maintain such insurance in adequate amounts, or on acceptable terms, to provide coverage against potential liabilities. The product liability coverage we currently have for our clinical trials may be insufficient to cover fully the costs of any claim or any ultimate damages we may be required to pay. Our inability to obtain or maintain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or limit the commercialization of any products we develop, and could leave us exposed to significant financial losses relating to any products that we do develop and commercialize.

***If we use hazardous or biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.***

Our research and development activities involve the controlled use of potentially hazardous substances, including toxic chemical and biological materials. Our operations produce hazardous waste products. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of these hazardous and biological materials. While we believe that we are currently in compliance with these laws and regulations, continued compliance may be expensive, and current and future environmental regulations may impair our research, development and manufacturing efforts. In addition, if we fail to comply with these laws and regulations at any point in the future, we may be subject to criminal sanctions and substantial civil liabilities and could be required to suspend or modify our operations. Even if we continue to comply with all applicable laws and regulations regarding hazardous materials, we cannot eliminate the risk of accidental contamination or discharge and our resultant liability for any injuries or other damages caused by these accidents. Although we maintain general liability insurance, this insurance may not fully cover potential liabilities for these damages, and the amount of uninsured liabilities may exceed our financial resources and materially harm our business.

***The FDA approval process for drugs involves substantial time, effort and financial resources, and we may not receive any new approvals for our product candidates on a timely basis, or at all.***

The process required by the FDA before product candidates may be marketed in the U.S. generally involves the following:

- preclinical laboratory and animal testing;
- submission of an IND application which must become effective before clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of proposed drugs or biologics for their intended use;
- pre-approval inspection of manufacturing facilities, company regulatory files and selected clinical investigators; and
- FDA approval of a new drug application, or NDA, or FDA approval of an NDA supplement in the case of a new indication if the product is already approved for another indication.

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The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any new approvals for our product candidates will be granted on a timely basis, if at all. We have failed in the past, and may in the future fail, to make timely submissions of required reports or modifications to clinical trial documents, and such delays as well as possible errors or omissions in such submissions could endanger regulatory acceptance of clinical trial results or even our ability to continue with our clinical trials.

The results of product development, preclinical tests and clinical trials are submitted to the FDA as part of an NDA, or as part of an NDA supplement. The FDA may deny approval of an NDA or NDA supplement if the applicable regulatory criteria are not satisfied, or it may require additional clinical data or an additional pivotal Phase III clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA or NDA supplement does not satisfy the criteria for approval. The FDA may move to withdraw product approval, once issued, if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA may move to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory agencies typically takes several years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease. Government regulation may delay or prevent marketing of product candidates for new indications for a considerable period of time and impose costly procedures upon our activities. The FDA or any other regulatory agency may not grant approvals for new indications for our product candidates on a timely basis, if at all.

Success in early stage clinical trials does not ensure success in later stage clinical trials. Data obtained from clinical trials is not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Even if a product candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations and dosages. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Delays in obtaining, or failures to obtain, additional regulatory approvals for our products would harm our business. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

The FDA s policies may change and additional government regulations may be enacted, which could prevent or delay regulatory approval of our product candidates or approval of new indications for our product candidates. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the U.S. or internationally.

***If we or our contract manufacturers fail to comply with applicable regulations, sales of our products could be delayed and our revenue could be harmed.***

Every medical product manufacturer is required to demonstrate and maintain compliance with cGMP. We and any third party manufacturers or suppliers with whom we enter into agreements will be required to meet these requirements. Our contract manufacturers will be subject to unannounced inspections by the FDA and corresponding foreign and state agencies to ensure strict compliance with cGMP and other applicable government quality control and record-keeping regulations. In addition, transfer of ownership of products triggers a mandatory manufacturing inspection requirement from the FDA. We cannot be certain that we or our contract manufacturers will pass any of these inspections. If we or our contract manufacturers fail one of these inspections in the future, our operations could be disrupted and our manufacturing and sales delayed significantly until we can demonstrate adequate compliance. If we or our contract manufacturers fail to take adequate corrective action in a timely fashion in response to a quality system regulations inspection, the FDA could shut down our or our contract manufacturers manufacturing operations and require us, among other things, to recall our products, either of which would harm our business.

Failure to comply with cGMP or other applicable legal requirements can lead to federal seizure of violative products, injunctive actions brought by the federal government, and potential criminal and civil liability on the part of a company and its officers and employees. Because of these and other factors, we may not be able to replace our manufacturing capacity quickly or efficiently in the event that our contract manufacturers are unable to manufacture our products at one or more of their facilities. As a result, the sale and marketing of our products could be delayed or

we could be forced to develop our own manufacturing capacity, which would require substantial additional funds and personnel