MEDICINOVA INC
Form S-1
September 01, 2005
**Table of Contents**

**As filed with the United States Securities and Exchange Commission on September 1, 2005**

**Registration No. 333-**

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# UNITED STATES

# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

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# FORM S-1

# REGISTRATION STATEMENT

***Under***

***The Securities Act of 1933***

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# MediciNova, Inc.

**(Exact Name of Registrant as Specified in Its Charter)**

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| **Delaware** | **2834** | **33-0927979** |
|---|---|---|
| **(State or Other Jurisdiction of Incorporation or Organization)** | **(Primary Standard Industrial Classification Code Number)** | **(I.R.S. Employer Identification Number)** |

**4350 La Jolla Village Drive, Suite 950**

**San Diego, CA 92122**

**(858) 373-1500**

**(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant s Principal Executive Offices)**

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**Takashi Kiyoizumi, M.D., Ph.D.**

**MediciNova, Inc.**

**President and Chief Executive Officer**

**4350 La Jolla Village Drive, Suite 950**

**San Diego, CA 92122**

**(858) 373-1500**

**(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent For Service)**

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***Copy to:***

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**Approximate date of commencement of proposed sale to the public:** From time to time after the effective date of this registration statement.

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. ¨

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. ¨

If this form is a post-effective amendment filed pursuant to Rule 462(d) 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. ¨

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. ¨

**CALCULATION OF REGISTRATION FEE**

| Title of Each Class of Securities To Be Registered | Amount To Be Registered | Proposed Maximum Offering Price Per Share(1) | Proposed Maximum Aggregate Offering Price(1) | Amount Of Registration Fee |
|---|---|---|---|---|
| Common Stock, $0.001 par value per share | 67,282,856 shares | $ 1.77 | $ 119,090,656 | $ 14,017 |

(1) Estimated based upon the average of the high and low sales prices of the Registrant s common stock on August 31, 2005, as reported by the Hercules Market of the Osaka Securities Exchange, solely for the purpose of calculating the registration fee pursuant to Rule 457(o) promulgated under the Securities Act of 1933. On August 31, 2005, the exchange rate for the Japanese Yen was 111 Yen per U.S. Dollar, as quoted on www.oanda.com.

**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, or until this registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.**

**Table of Contents**

**The information contained in this prospectus is not complete and may be changed. The selling stockholders 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 it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.**

**PROSPECTUS**

**(SUBJECT TO COMPLETION, DATED SEPTEMBER 1, 2005)**

# 67,282,856 Shares

# MEDICINOVA, INC.

## Common Stock

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This prospectus relates to an aggregate of up to 67,282,856 shares of our common stock which may be offered by the selling stockholders identified in this prospectus for their own account. The prices at which the selling stockholders may sell the shares will be determined by the prevailing market for the shares or in negotiated transactions. We will not receive any proceeds from the sale of shares offered by this prospectus.

Our common stock is quoted on the Hercules Market of the Osaka Securities Exchange under the symbol 4875. On August 31, 2005, the last reported sale price of our common stock was 197 Japanese Yen (or approximately $1.77) per share (based on an exchange rate of 111 Yen per U.S. Dollar, as quoted on www.oanda.com).

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**The shares of common stock offered or sold under this prospectus involve a high degree of risk. You should carefully consider the Risk Factors beginning on page 4 of this prospectus before purchasing any of the shares of common stock offered by this prospectus.**

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

The date of this prospectus is September , 2005

Table of Contents

**TABLE OF CONTENTS**



**You should rely only on information contained in this prospectus. We have not authorized any person to provide you with information that differs from what is contained in this prospectus. If any person does provide you with information that differs from what is contained in this prospectus, you should not rely on it. This prospectus is not an offer to sell or the solicitation of an offer to buy any securities other than the securities to which it relates, or an offer of solicitation in any jurisdiction where offers or sales are not permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, even though this prospectus may be delivered or shares may be sold under this prospectus on a later date.**

*References in this prospectus to we, our, us, the Company and MediciNova refer to MediciNova, Inc., a Delaware corporation.*

*This prospectus refers to trademarks and trade names we own, as well as those owned by other companies. MediciNova is a registered trademark that we own in the United States and Japan. Each other trademark or trade name appearing in this prospectus belongs to its respective owner.*

Table of Contents

**MEDICINOVA, INC.**

**PROSPECTUS SUMMARY**

*The information contained in this summary is qualified in its entirety by, and should be read in conjunction with, the detailed information and financial statements, including the notes thereto, appearing elsewhere in this prospectus. You should read the following summary together with the more detailed information, including Risk Factors and our financial statements and related notes, before making your investment decision.*

**Our Business**

We are a specialty pharmaceutical company focused on acquiring, developing and commercializing innovative pharmaceutical products for a variety of diseases and conditions. We actively seek to identify and acquire license rights to product candidates with extensive safety and efficacy data that are in late pre-clinical or early clinical development and that address large markets with significant opportunities for improved therapies.

Our development programs follow a dual pathway:

strategic core programs; and

partnering programs.

Our strategic core programs consist of product candidates to which we intend to retain the rights through final regulatory approval in the United States and commercialize directly. Our partnering programs consist of product candidates we intend to license to larger pharmaceutical companies and with respect to which we intend to retain co-promotion rights. To date, we have acquired license rights to six compounds for the development of seven product candidates. In our strategic core programs, currently we have Phase I clinical trials ongoing for MN-221 (premature labor), we have Phase I clinical trials ongoing and have initiated a Second Phase I clinical trial for MN-029 (solid tumor) and we intend to enter into a Phase I clinical trial for MN-246 (urinary incontinence; pollakisuria) during the first quarter of 2006. Currently we have Phase II clinical trials ongoing for MN-001 (interstitial cystitis) in our strategic core programs and for MN-305 (Generalized Anxiety Disorder), MN-001 (bronchial asthma) and MN-166 (multiple sclerosis) in our partnering programs.

We have assembled a management team with extensive experience in the pharmaceutical and biotechnology industry, including experience in pre-clinical research, drug substance and product preparation, regulatory affairs, clinical research, marketing and sales and corporate development. We have successfully utilized our expertise to generate revenues from development management contracts with Asahi Kasei Pharma Corporation and Argenes Inc., both Japanese pharmaceutical companies, for consulting services rendered. We intend to seek similar revenue opportunities to augment our dual pathway development approach and to provide us with additional in-license opportunities.

**Our Strategy**

Our goal is to become a leader in the development and commercialization of drugs for the treatment of diseases with unmet medical needs. Key elements of our strategy are to:

execute our dual pathway development approach;

continue to expand our pipeline of promising product candidates;

partner selectively with larger pharmaceutical companies to maximize the commercial potential of our product candidates; and

continue to strengthen our management team.

Table of Contents

**Our History**

We were founded in September 2000 by Takashi Kiyoizumi, M.D., Ph.D. and Yuichi Iwaki, M.D., Ph.D. as a majority-owned subsidiary of the Japanese pharmaceutical company, Tanabe Seiyaku Co., Ltd. Prior to joining MediciNova, Dr. Kiyoizumi had been the chief executive of Tanabe Research Laboratories, USA, the San Diego-based research arm of Tanabe Seiyaku. Our operations are now completely independent of Tanabe Seiyaku, which, as of June 30, 2005, indirectly owned approximately 10% of our outstanding capital stock.

Our principal executive offices are located at 4350 La Jolla Village Drive, Suite 950, San Diego, California 92122, and our telephone number is (858) 373-1500. Our website address is www.medicinova.com. The information on our website is not incorporated into this prospectus.

On February 4, 2005, we completed an initial public offering, or IPO, of 30 million shares of common stock for proceeds of $104.5 million, net of underwriting discounts and commissions and offering expenses. On February 8, 2005, our common stock was listed and began trading on the Hercules Market of the Osaka Securities Exchange.

On March 8, 2005, we completed the sale of 1,573,000 shares of our common stock for aggregate proceeds of $5.6 million, net of underwriting discounts and commissions. The sale of these shares was the result of the underwriters partial exercise of the over-allotment option we granted to them in connection with our IPO.

**Risks Affecting Our Business and Strategy**

Our business and the success of our strategy are subject to numerous risks, which are highlighted in the section entitled Risk Factors immediately following this prospectus summary, including the following:

- we are a development stage company with a limited operating history and limited revenues derived from operations;
- we have incurred significant losses since our inception, and at June 30, 2005, our cumulative net loss was approximately $75.5 million, including $34.5 million of non-cash stock-based compensation expense related to employee stock-based compensation and founders warrants;
- we expect to incur substantial net losses for the next several years as we continue to develop our existing programs, expand our research and development programs and acquire or in-license products, technologies or businesses that are complementary to our own;
- we do not have any products that are approved for sale;
- we may be unsuccessful in developing and gaining regulatory approval for new product candidates, we may not be able to sustain our operations and we may never become profitable;

if we are unable to retain key management members or expand our management team, we may be unable to successfully develop or commercialize our product candidates as planned;

if we fail to identify and license or acquire other product candidates, we will not be able to grow our business; and

we may need additional financing to execute our strategy to acquire, develop and commercialize product candidates.

Table of Contents

**The Offering**

Since our inception, we have issued a total of 28,959,006 shares of preferred stock. In October 2000 and August 2001, we issued and sold a total of 1,000,000 shares of Series A preferred stock for aggregate net proceeds of $10 million, from March 2003 through May 2004, we issued and sold 291,150 shares of Series B preferred stock for aggregate net proceeds of $26.8 million and on September 2, 2004, we issued and sold 27,667,856 shares of Series C preferred stock for aggregate net proceeds of $43.4 million. Upon the consummation of our IPO, all of our preferred stock was converted into an aggregate of 66,782,856 shares of our common stock. Together with 500,000 shares of common stock held by our founders, we have outstanding 67,282,856 shares of restricted common stock. The holders of such shares generally have rights to cause us to file one or more registration statements on their behalf pursuant to a registration rights agreement that we entered into with these stockholders. We voluntarily are filing this prospectus with respect to such shares, and the prices at which the selling stockholders may sell their shares will be determined by the prevailing market for the shares or in negotiated transactions. We also have 13,356,572 shares of unregistered common stock subject to unexercised in-the-money warrants that are not being registered for resale at this time but may be sold pursuant to Rule 144 under the Securities Act of 1933, subject to the volume restrictions imposed by Rule 144. Of this amount, 12,856,572 shares are subject to warrants held by our founders.

Table of Contents

## RISK FACTORS

*We operate in a dynamic and rapidly changing environment that involves numerous risks and uncertainties. An investment in our common stock involves significant risk. The following section describes some, but not all, of the risks and uncertainties that may have a material adverse affect on our business, financial condition, results of operations and the market price of our common stock and that could cause our actual results to differ materially from those expressed or implied in our forward-looking statements. You should carefully consider the following risks and all the other information in this prospectus before you decide to buy our common stock.*

### Risks Related to Our Business

***We expect our net losses to continue for at least several years and we are unable to predict the extent of our losses.***

We are a development stage specialty pharmaceutical company with a limited operating history. We have incurred significant net losses since our inception. For the year ended December 31, 2004, we had a net loss of $48.3 million, including $34.3 million of non-cash stock-based compensation charges. For the six months ended June 30, 2005, we had a net loss of $12.0 million. We expect our annual net losses, exclusive of stock-based compensation charges, to increase over the next several years as we expand and incur significant clinical development costs. These losses have reduced our stockholders equity and will continue to reduce our stockholders equity and working capital.

We expect our development expenses to increase in connection with our planned clinical trials for our product candidates and any other development projects that we may initiate. In addition, we expect to incur increased general and administrative expenses as well as the increased costs to operate as a public company. Consequently, we expect to continue to incur significant and increasing operating losses, exclusive of stock-based compensation charges, for the foreseeable future.

***We do not have any products that are approved for commercial sale and therefore do not expect to generate any revenues from product sales in the foreseeable future.***

We have not received, and do not expect to receive for at least the next several years, any revenues from the commercialization of our product candidates. To date, we have not generated any product revenue and have funded our operations primarily from sales of our securities. Our only source of revenues since inception has been from development management services rendered to Asahi Kasei Pharma Corporation and Argenes Inc., both Japanese pharmaceutical companies, in connection with their clinical development of pharmaceutical product candidates. Our contract with Asahi Kasei Pharma has been completed and we do not expect to generate further revenues from that agreement. We anticipate that we will continue to receive modest revenues for rendering consulting services and that, prior to our commercialization of a product candidate, our consulting revenues, together with out-licensing upfront and milestone payments, will be our primary source of revenues. To obtain revenues from sales of our product candidates, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, and manufacturing and marketing drugs with market potential. We may never succeed in these activities, and may not generate sufficient revenues to continue our business operations or achieve profitability.

***The loss of any rights to develop and market any of our product candidates would significantly impair our operating results.***

We license the rights to develop and market our product candidates. Currently, we have licensed six compounds for the development of seven product candidates. They are:

MN-221 for premature labor licensed from Kissei Pharmaceutical;

Table of Contents

MN-029 for solid tumors licensed from Angiogene Pharmaceuticals;

MN-001 for interstitial cystisis and asthma licensed from Kyorin Pharmaceutical;

MN-305 for anxiety licensed from Mitsubishi Pharma Corporation;

MN-166 for multiple sclerosis licensed from Kyorin Pharmaceutical; and

MN-246 for urinary incontinence licensed from Mitsubishi Pharma Corporation.

We are obligated to develop and commercialize these product candidates in accordance with mutually agreed upon terms and conditions. Our ability to satisfy some or all of the terms and conditions of our licensing arrangements is dependent on numerous factors, including some factors that are outside of our control. Our licensing arrangements may be terminated if we breach our obligations under the agreements materially and fail to cure a breach within a specified period of time.

If any of our license agreements is terminated, we would have no further rights to develop and commercialize the product candidate which is the subject of the license. The termination of any of our license agreements would significantly and adversely affect our business.

***In order to commercialize a therapeutic drug successfully, a product candidate must undergo clinical trials, which are long, complex and costly, manifest a high risk of failure and can be delayed or suspended.***

Six of our seven product candidates are in clinical development, the process that is required to receive regulatory approval for commercial sale. The regulatory approval process is long, complex and costly. It may take several years to complete the clinical development necessary to commercialize a drug, and delays or failure can occur at any stage which may result in our inability to market and sell products derived from our product candidates and to generate product revenues. Of the large number of drugs in development, only a small percentage result in the submission of a new drug application to the Food and Drug Administration, or FDA, and even fewer are approved for commercialization. Interim results of clinical trials do not necessarily predict final results, and success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials even after promising results in earlier trials.

In connection with clinical trials, we face risks that:

a product candidate may not prove to be efficacious;

patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested;

the results may not confirm the positive results of earlier trials; and

the results may not be acceptable to the FDA or other regulatory agencies.

To date, the FDA has accepted Investigational New Drug, or IND, applications for five of our seven product candidates. We have filed Clinical Trial Authorization, or CTA, applications, the equivalent of a U.S. IND, in nine European countries to conduct a Phase II study for MN-166 in patients with multiple sclerosis. Four of these applications are approved and the remaining five are under active review. We cannot conduct human clinical trials in the United States or in Eastern Europe on our remaining product candidate until an IND or CTA application is in effect and there can be no assurance that the regulatory authorities, including the FDA, will allow our applications to go into effect.

The commencement of clinical trials can be delayed for a variety of other reasons, including delays in:

demonstrating sufficient safety to persuade regulatory authorities to allow a clinical trial to begin;

Table of Contents

- reaching agreement on acceptable terms with prospective contract research organizations and clinical trial sites;
- manufacturing sufficient quantities of a product candidate;
- obtaining institutional review board approval to conduct a clinical trial at a prospective site; and
- obtaining sufficient patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial.

Once a clinical trial has begun, it may be delayed, suspended or terminated due to a number of factors, including:

- ongoing discussions with regulatory authorities regarding the scope or design of our clinical trials or requests by them for supplemental information with respect to our clinical trial results;
- our failure or inability to conduct clinical trials in accordance with regulatory requirements;
- lower than anticipated retention rates of patients in clinical trials;
- serious adverse events or side effects experienced by participants; or
- insufficient supply or deficient quality of product candidates or other materials necessary for the conduct of our clinical trials.

Many of these factors described above may also ultimately lead to denial of regulatory approval of a current or potential product candidate. If we experience delays in our clinical trials, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenues will be delayed.

***If we fail to identify and license or acquire other product candidates, we will not be able to expand our business.***

Since we have limited internal discovery capabilities, our business is substantially dependent on our ability to license or acquire late preclinical-stage or early clinical-stage product candidates and further develop them for commercialization. The success of this strategy depends upon our ability to identify, select and acquire the right product candidates. We have limited experience identifying, negotiating and implementing economically viable product candidate acquisitions or licenses, which is a lengthy and complex process. Also, the market for licensing and acquiring product candidates is intensely competitive and many of our competitors have greater resources than us. We may not have the requisite capital resources to consummate product candidate acquisitions or licenses that we identify to fulfill our strategy.

Moreover, product candidate acquisitions that we do complete involve numerous risks, including:

difficulties in integrating the development program for the acquired product candidate into our existing operations;

diversion of financial and management resources from existing operations;

risks of entering new markets or technologies;

inability to generate sufficient revenues to offset acquisition costs; and

delays that may result from us having to perform unanticipated pre-clinical trials or other tests on the product candidate.

If we are not successful in identifying and licensing or acquiring other product candidates, we will not be able to grow our revenues with sales from new products.

Table of Contents

***If we fail to obtain the capital necessary to fund our operations, we will be unable to develop and commercialize our product candidates.***

We have consumed substantial amounts of capital since our inception. From our inception to June 30, 2005, we used $38.5 million in cash to fund our operating activities and acquisitions of property and equipment. Although we believe our existing cash and investments will be sufficient to fund our anticipated cash requirements through 2006, we will require significant additional financing in the future to fund our operations. Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- progress in, and the costs of, our clinical trials;
- the costs of securing manufacturing arrangements for clinical or commercial production;
- the costs involved in filing, prosecuting, enforcing and defending patent claims and other intellectual property rights; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approval to market our product candidates.

Until we can generate significant continuing revenues, we expect to satisfy our cash needs through strategic collaborations, private or public sales of our securities, debt financings or by licensing all or a portion of our product candidates. We cannot be certain that additional sources of capital will be available to us on acceptable terms, or at all. If sources of capital are not available, we may not be in a position to pursue other business opportunities that require financial commitments and we may be required to:

- terminate or delay clinical trials for one or more of our product candidates;
- delay establishing sales and marketing capabilities;
- curtail our efforts to acquire new product candidates; or
- relinquish rights to our technologies or product candidates.

***The terms under which we raise additional capital may adversely affect our business and may significantly dilute stockholders ownership interests.***

If we raise additional funds through collaborations or licensing arrangements with third parties, we may need to relinquish some rights to our product candidates, including commercialization rights, that may adversely affect our ability to grow our business. If we raise additional funds by issuing equity securities, stockholders may experience substantial dilution. Debt financing, if available, may involve restrictive covenants. Any debt financing or additional equity that we raise may contain terms that are not favorable to us or our stockholders.

***We will depend on strategic collaborations with third parties to develop and commercialize selected product candidates and will not have control over a number of key elements relating to the development and commercialization of these product candidates.***

A key aspect of our strategy is to enter into collaborations with third-party partners whereby we license selected product candidates to larger pharmaceutical companies that are willing to conduct later-stage clinical trials and further develop and commercialize those products. To date, we have not entered into any collaborative arrangements with any third-party partners and currently do not expect to do so until we have successfully completed further studies for at least one of our partnering program product candidates.

By entering into these strategic collaborations, we may rely on our partners for financial resources and for development, commercialization and regulatory expertise. Our partners may fail to develop or effectively commercialize products using our product candidates because they:

- do not have sufficient resources or decide not to devote the necessary resources due to internal constraints such as limited cash or human resources;

Table of Contents

- decide to pursue a competitive potential product that has been developed outside of the collaboration; or

- cannot obtain the necessary regulatory approvals.

We may not be able to enter into collaborations on acceptable terms, if at all. We also face competition in our search for partners with whom we may collaborate.

***We rely on third parties to conduct our clinical trials and perform data collection and analysis, which may result in costs and delays that may hamper our ability to successfully develop and commercialize our product candidates.***

Although we design and manage our current clinical trials, we do not have the ability to conduct clinical trials directly for our product candidates. We will rely on contract research organizations, medical institutions, clinical investigators and contract laboratories to conduct our clinical trials and to perform data collection and analysis. In the course of clinical development, we have contracted and will continue to contract with a number of these research organizations, including, without limitation, MDS Pharma Services of Belfast, Northern Ireland; Pharmaceutical Research Associates, Inc. of Lenexa, Kansas; Fulcrum Pharma Developments, Inc. of Durham, North Carolina; Paragon, Inc. of Irvine, California; and Quintiles, Inc. of Morrisville, North Carolina.

Our clinical trials may be delayed, suspended or terminated if:

- the third parties upon whom we rely do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines;

- such third parties need to be replaced; or

- the quality or accuracy of the data obtained by the third parties is compromised due to their failure to adhere to our clinical protocols or regulatory requirements or for other reasons.

Failure to perform by the third parties upon whom we rely may increase our development costs, delay our ability to obtain regulatory approval and prevent the commercialization of our product candidates. While we believe that there are numerous alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without delays or additional expenditures.

***Our product candidates, if approved for sale, may not gain acceptance among physicians, patients and the medical community, thereby limiting our potential to generate revenues.***

Even if our product candidates are approved for commercial sale by the FDA or other regulatory authorities, the degree of market acceptance of any approved product candidate by physicians, healthcare professionals and third-party payors and our profitability and growth will depend on a number of factors, including:

relative convenience and ease of administration;

the prevalence and severity of any adverse side effects;

availability of alternative treatments;

pricing and cost effectiveness, which may be subject to regulatory control;

effectiveness of our or any of our partners sales and marketing strategies; and

our ability to obtain sufficient third-party insurance coverage or reimbursement.

If any product candidate that we develop does not provide a treatment regimen that is as beneficial as the current standard of care or otherwise does not provide patient benefit, that product candidate likely will not be approved by relevant regulatory authorities or, if approved, achieve market acceptance.

Table of Contents

***We are dependent on our management team, particularly Takashi Kiyoizumi, M.D., Ph.D., a founder and our chief executive officer, and Yuichi Iwaki, M.D., Ph.D., a founder and executive chairman of our board of directors, and if we are unable to attract, retain and motivate these and other key management and scientific staff our drug development programs may be delayed and we may be unable to successfully develop or commercialize our product candidates.***

We are dependent upon the continued services of our executive officers and other key personnel, particularly Takashi Kiyoizumi, M.D., Ph.D., one of our founders and our chief executive officer, and Yuichi Iwaki, M.D., Ph.D, one of our founders and the executive chairman of our board of directors, who have been instrumental in our ability to in-license product candidates from Japanese pharmaceutical companies and secure financing from Japanese institutions. The relationships that our key managers have cultivated with pharmaceutical companies from whom we license product candidates and to whom we expect to out-license product candidates as part of our partnering program make us particularly dependent upon their continued employment with us. We are also substantially dependent on the continued services of our existing project management personnel because of the highly technical nature of our product development programs.

As we acquire or license new product candidates, our success will depend on our ability to attract, retain and motivate highly qualified management and scientific personnel to manage the development of these new product candidates. In particular, our drug development programs depend on our ability to attract and retain highly experienced development and regulatory personnel. In addition, we will need to hire additional personnel as we continue to expand our clinical development and other development activities. If we are successful in developing candidates for commercialization, we will need to hire additional personnel to direct those activities as well. We face competition for experienced scientists and other technical and professional personnel from numerous companies and academic and other research institutions. Competition for qualified personnel is particularly intense in the San Diego, California area, where our offices are located. Our short operating history and the uncertainties attendant to being a development-stage specialty pharmaceutical company with limited capital resources could impair our ability to attract and retain personnel and impede the achievement of our development and commercialization objectives.

Although we have employment agreements with key members of management, each of our employees may terminate his or her employment at any time. If we lose any of our key management personnel, we may not be able to find suitable replacements and our business would be harmed as a result.

***If we are unable to establish our sales and distribution capabilities, we will be unable to successfully commercialize our core product candidates.***

To date, we have not sold, marketed or distributed any pharmaceutical products. If we are successful in developing and obtaining regulatory approvals for the product candidates in our strategic core programs or acquire other products, we will need to establish sales, marketing and distribution capabilities. Developing an effective sales and marketing force will require a significant amount of our financial resources and time. We may be unable to establish and manage an effective sales force in a timely or cost-effective manner, if at all, and any sales force we do establish may not be capable of generating demand for our products. Although we intend to establish strategic collaborations to market the products in our strategic core programs outside the United States, if we are unable to establish such collaborations, we may be required to market our strategic core product candidates outside of the United States directly. In that event, we may need to build a corresponding international sales and marketing capability with technical expertise and supporting distribution capabilities.

***We will need to increase the size of our organization, and we may encounter difficulties managing our growth, which could adversely affect our results of operations.***

We will need to expand and effectively manage our operations and facilities in order to advance our drug development programs, achieve milestones under our collaboration agreements, facilitate additional

Table of Contents

collaborations and pursue other development activities. For example, we intend to hire additional personnel in clinical development, regulatory affairs and corporate development to further strengthen our core competencies. Similarly, we are likely to hire additional management and administrative personnel to manage our business and affairs as we continue to grow. In addition, we will have to develop sales, marketing and distribution capabilities for the product candidates in our strategic core programs. The scope and timing of these hires is highly uncertain and remains subject to the success of our current product candidate development programs.

To manage our growth, we will be required to continue to improve our operational, financial and management controls, reporting systems and procedures and to attract and retain sufficient numbers of talented employees. Meeting our public reporting obligations and other regulatory requirements in the United States and Japan now that we are a public company will place additional demands on our limited resources. We may not successfully manage the expansion of our operations and, accordingly, may not achieve our development and commercialization goals.

***We expect that our results of operations will fluctuate, which may make it difficult to predict our performance from period to period.***

Our quarterly operating results have fluctuated in the past and likely will continue to fluctuate. Some of the factors that could cause our operating results to fluctuate include:

- the status of development of our product candidates and, particularly, the timing of any milestone payments to be paid or received by us under our licensing agreements;
- the incurrence of clinical expenses that could fluctuate significantly from period to period;
- the unpredictable effects of collaborations during these periods;
- the timing of our satisfaction of applicable regulatory requirements, if at all;
- the rate of expansion of our clinical development and other internal development efforts;
- the effect of competing technologies and products and market developments;
- stock-based compensation expense associated with stock options we may grant in the future; and
- general and industry-specific economic conditions.

We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

***Relying on third-party manufacturers may result in delays in our clinical trials and product introductions as well as increased costs.***

We have no manufacturing facilities, and we do not intend to develop facilities for the manufacture of product candidates for clinical trials or commercial purposes in the foreseeable future. We are contracting with third-party manufacturers to produce, in collaboration with us, sufficient quantities of our product candidates for clinical trials. While we believe that there are competitive sources available to manufacture our product candidates, we may not be able to enter into arrangements without delays or additional expenditures. We cannot estimate these delays or costs with certainty. To date, these manufacturers have met the requirements of our programs; however, we have only required our product candidates in very limited volume because we do not have any commercialized product.

Our manufacturers will be obliged to operate in accordance with FDA-mandated or International Convention on Harmonization (ICH) current good manufacturing practices, or cGMPs. A failure of any of our contract manufacturers to establish and follow cGMPs and to document their adherence to such practices may lead to significant delays in clinical trials or in obtaining regulatory approval of product candidates or the ultimate launch of our products into the market. In addition, changing contract manufacturers is difficult. For example, doing so requires re-validation of the manufacturing processes and procedures in accordance with

Table of Contents

cGMPs, which may be costly and time-consuming. Failure by our third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of the government to grant pre-market approval of drugs, delays, suspension or withdrawal of approvals, seizures or recalls of products, operating restrictions and criminal prosecutions.

***We may not be able to manufacture our product candidates in commercial quantities, which would prevent us from commercializing our product candidates.***

To date, our product candidates have been manufactured in small quantities for pre-clinical and clinical trials. If any of these product candidates are approved by the FDA or other regulatory agencies for commercial sale, we will need to manufacture them in larger quantities. We may not be able successfully to increase the manufacturing capacity, whether in collaboration with third-party manufacturers or on our own, for any of our product candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. If we are unable to successfully increase the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed or there may be a shortage in supply. Our product candidates will require precise, high-quality manufacturing. Our failure to achieve and maintain these high manufacturing standards, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could result in a material adverse effect on our business, financial condition and results of operations.

***Materials necessary to manufacture our products may not be available on commercially reasonable terms, or at all, which may delay the development and commercialization of our products.***

We rely on the manufacturers for our products to purchase from third-party suppliers the materials necessary to produce the compounds for our clinical trials and, if we obtain marketing approval for any of our products, for commercial distribution. Suppliers may not sell these materials to our manufacturers at the time we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers. Moreover, we currently do not have any agreements for the production of these materials. If our manufacturers are unable to obtain these materials for our clinical trials, product testing and potential regulatory approval of our products would be delayed, significantly impacting our ability to develop the product candidate. If our manufacturers or we are unable to purchase these materials after regulatory approval has been obtained, the commercial launch of any effected product would be delayed, or there would be a shortage in supply of any such product, which would materially affect our ability to generate revenues from the sale of any such product.

***If the holders of the shares offered by this prospectus were to determine to sell all or a significant portion of their shares at one time, there would be significant downward pressure on our stock price and it may be difficult to sell your shares.***

We are registering 67,282,856 shares for resale in this offering, which shares are being held by 46 stockholders. Currently, approximately 31.5 million of our shares are trading in the public markets.

The trading volume for our stock is extremely low, with an average volume of approximately 87,000 shares per day during the last four weeks. If the holders of the shares offered by this prospectus were to decide to immediately sell their shares, there would be significant downward pressure on our stock price and it may be difficult, or even impossible, to find a buyer for shares of our common stock you may wish to sell immediately. In addition, 12,856,572 shares of our common stock may be issued upon exercise of warrants held by our founders at an exercise price of $0.10 per share and 500,000 shares of common stock may be issued upon exercise of a warrant held by another person at an exercise price of $1.00 per share. The warrants held by our founders expire in 2007 and the warrant held by the other party expires in 2009. If these

warrants are exercised, our stockholders will experience immediate and substantial dilution. In addition, upon sale of these shares, which may be sold pursuant to the volume limitations of Rule 144, the market value of our common stock may decline if there is insufficient demand in the public markets to purchase the shares.

Table of Contents

***Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us more complicated and the removal and replacement of our directors and management more difficult.***

Our restated certificate of incorporation and amended and restated bylaws contain provisions that may delay or prevent a change in control, discourage bids at a premium over the market price of our common stock or adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. These provisions may also make it difficult for stockholders to remove and replace our board of directors and management. These provisions:

- establish that members of the board of directors may be removed only for cause upon the affirmative vote of stockholders owning at least a majority of our capital stock;
- authorize the issuance of blank check preferred stock that could be issued by our board of directors in a discriminatory fashion designed to increase the number of outstanding shares and prevent or delay a takeover attempt;
- limit who may call a special meeting of stockholders;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings;
- prohibit our stockholders from making certain changes to our restated certificate of incorporation or amended and restated bylaws except with 66 2/3% stockholder approval; and
- provide for a classified board of directors with staggered terms.

We also are subject to provisions of the Delaware corporation law that, in general, prohibit any business combination with a beneficial owner of 15% or more of our common stock for three years unless the holder s acquisition of our stock was approved in advance by our board of directors.

Although we believe these provisions collectively provide for an opportunity to receive higher bids by requiring potential acquirors to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders. In any event, these provisions may delay or prevent a third party from acquiring us and any such delay or prevention could cause the market price of our common stock to decline.

***We have never paid dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future.***

We have paid no cash dividends on any of our classes of capital stock to date and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of existing or any future debt may preclude us from paying these dividends. As a result, appreciation in the market value, if any, of our common stock will be our stockholders sole source of gain for the foreseeable future. The market value for our common stock has decreased since the time of our IPO, it may not hereafter increase, and in fact, the market value for our common stock may decrease further.

Any increase in the market value of our common stock is uncertain and unpredictable. Stockholders should not invest in our stock if they are seeking dividend income.

***Our financial outlook could be affected by changes in the accounting rules which govern the recognition of stock-based compensation expenses.***

We measure compensation expense for our employee stock compensation plans under the intrinsic value method of accounting prescribed by Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees. Under this method, in general, we incur expense equal to the difference, if any, between the exercise price of an option or warrant and the fair market value of the shares underlying the equity instrument on the date of grant. We amortize this expense over the vesting period of the equity instrument. For example, we

Table of Contents

incurred $0.2 million of stock based compensation in 2004 and $0.2 million for the six months ended June 30, 2005 related to stock option grants. In addition, we incurred $34.1 million of expense related to warrants we issued to our founders. The Financial Accounting Standards Board has announced changes to accounting rules concerning the reco