

MAP Pharmaceuticals, Inc.  
Form 424B5  
September 30, 2010  
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Filed Pursuant to Rule 424(b)(5)

Registration No. 333-164894

**Prospectus Supplement**

(to Prospectus Dated April 16, 2010)

## **MAP Pharmaceuticals, Inc.**

### **3,000,000 Shares of Common Stock**

We are offering 3,000,000 shares of our common stock.

Our common stock is listed on The Nasdaq Global Market under the symbol MAPP. The last reported sales price of our common stock on September 28, 2010 was \$15.19 per share.

**Investing in our common stock involves significant risks. See Risk Factors beginning on page S-5 of this prospectus supplement and page 1 of the accompanying prospectus.**

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement. Any representation to the contrary is a criminal offense.**

	<b>Per Share</b>	<b>Total</b>
Public Offering price	\$ 14.50	\$ 43,500,000
Underwriting discounts and commissions	\$ 0.725	\$ 2,175,000
Proceeds, before expenses, to us	\$ 13.775	\$ 41,325,000

We estimate the total expenses of this offering, excluding the underwriting discounts and commissions, will be approximately \$450,000. The underwriters may also purchase up to an additional 450,000 of our common shares from us at the public offering price, less underwriting discounts and commissions, to cover over-allotments, if any, within 30 days of the date of this prospectus supplement.

We anticipate that delivery of the shares of our common stock will be made through the facilities of the Depository Trust Company on or about October 4, 2010, subject to customary closing conditions.

*Sole Book-Running Manager*

**Lazard Capital Markets**

*Co-Manager*

**Wedbush PacGrow Life Sciences**

Prospectus supplement dated September 29, 2010.

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**ABOUT THIS PROSPECTUS SUPPLEMENT**

This prospectus supplement and the accompanying prospectus are part of a registration statement that we filed with the Securities and Exchange Commission (the "SEC") using a shelf registration process. Under the registration statement, we registered the offering by us of up to \$100,000,000 of common shares, warrants, preference shares and debt securities for sale from time to time in one or more offerings. This prospectus supplement provides specific information about the offering by us of 3,000,000 of our common shares under the shelf registration statement, in addition to information concerning the over-allotment option granted by us.

Both this prospectus supplement and the accompanying prospectus include or incorporate by reference important information about us, our common stock and other information you should know before investing. You should read both this prospectus supplement and the accompanying prospectus as well as additional information described under "Where You Can Find More Information" elsewhere in this prospectus supplement.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with information that is different. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or a solicitation of an offer to buy by anyone in any jurisdiction in which such offer or solicitation is not authorized, or in which the person is not qualified to do so or to any person to whom it is unlawful to make such offer or solicitation. Neither the delivery of this prospectus supplement and the accompanying prospectus nor any sale hereunder shall, under any circumstances, create any implication that there has been no change in our affairs since the date of this prospectus supplement, that the information contained herein is correct as of any time subsequent to the date hereof or that any information incorporated or deemed to be incorporated by reference herein is correct as of any time subsequent to the date hereof.

This document is in two parts. The first part is the prospectus supplement, which adds to, updates or may change information contained in the accompanying prospectus. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. If information in this prospectus supplement is inconsistent with information in the accompanying prospectus, this prospectus supplement will apply and will supersede that information in the accompanying prospectus.

Information contained on our website does not constitute part of this prospectus supplement.

Unless the context indicates otherwise, references in this prospectus supplement to "MAP Pharmaceuticals," "we," "us," and "our" and the company to MAP Pharmaceuticals, Inc., its predecessors and its consolidated subsidiaries.

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**PROSPECTUS SUPPLEMENT SUMMARY**

*The following summary includes basic information about our company, this offering and information appearing elsewhere in this prospectus supplement and in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and may not contain all of the information that you should consider before investing in our common shares. For a more complete understanding of our company and this offering, we encourage you to read carefully this entire prospectus supplement and the accompanying prospectus, including the Risk Factors contained in this prospectus supplement, the accompanying prospectus and the financial documents and notes incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision. This prospectus supplement may add to, update or change information in the accompanying prospectus.*

**The Company**

Our goal is to use proprietary inhalation technologies to enhance the therapeutic benefits and commercial attractiveness of proven drugs while minimizing risk by capitalizing on their known safety, efficacy and commercialization history. We have proprietary product candidates in development that address large market opportunities, including our most advanced product candidate, LEVADEX, formerly known as MAP0004, our proprietary orally inhaled version of dihydroergotamine, or DHE, for the potential treatment of migraine. LEVADEX is designed to provide faster onset and longer lasting pain relief than triptans, the class of drugs most often prescribed for treating migraine.

For our LEVADEX migraine program, we expect to submit a new drug application, or NDA, to the U.S. Food and Drug Administration, or the FDA, in the first half of 2011. We initiated a Phase 3 clinical program in July 2008. In May 2009, we announced results of the efficacy portion of our first Phase 3 clinical trial of LEVADEX. We announced that the clinical trial met its four primary endpoints, pain relief and being nausea, phonophobia and photophobia free as reported two hours after dosing. Additional endpoints showed that LEVADEX provided rapid and sustained pain relief for up to 48 hours after dosing. In January 2010, the FDA informed us that a second pivotal efficacy study is not required for our LEVADEX NDA submission for the acute treatment of migraine if the topline efficacy results we submitted are confirmed during the review of our NDA. In order to obtain regulatory approval for LEVADEX, we will need to complete our remaining clinical studies, including our ongoing 12 month open-label safety extension of our Phase 3 clinical study and the analysis of the results of a thorough QT study.

The following summarizes the status of our LEVADEX clinical development program:

**Open-label safety trial:** This 12 month open-label, long-term safety extension of our Phase 3 FREEDOM-301 trial is designed to evaluate overall safety of LEVADEX in at least 300 patients for six months and 150 patients for 12 months, including asthmatics. To date, more than 400 patients have completed at least six months of treatment and more than 200 patients have completed twelve months of treatment. All non-asthmatic patients and a subset of asthmatic patients have completed treatment. The remaining patients are expected to complete treatment in 2010. We, along with an independent data monitoring committee, or DMC, recently completed an interim safety review of all patients, including asthmatics. In this trial, LEVADEX has been well tolerated and no drug-related serious adverse events have been reported. To date, no clinically significant trends have been reported for LEVADEX in the evaluation of cardiovascular measurements (as measured by electrocardiogram, echocardiogram and chest x-ray) and pulmonary function (as measured by DLco and FEV1).

**Thorough QT trial:** We have completed treatment in a randomized, double-blind, placebo-controlled, three-way, crossover trial of approximately 54 healthy adults that will evaluate whether LEVADEX has an effect on QT interval as measured by electrocardiogram. The objectives of the trial are to compare the acute effect of LEVADEX, moxifloxacin and placebo on the QT interval and assess the tolerability of a suprathreshold dose of LEVADEX. We anticipate releasing results from this trial in the fourth quarter of 2010.

**Pharmacodynamics (PD) trial:** This completed trial showed that there was no statistically significant difference between the LEVADEX orally inhaled migraine therapy and placebo groups in the primary endpoint of pulmonary artery pressure over two hours after administration. Pulmonary artery pressure in the intravenous DHE, or IV DHE, group was higher than both the LEVADEX and placebo groups. The PD trial was a randomized, double blind, placebo controlled, three-way, crossover trial in healthy adults, comparing the acute effects of LEVADEX, IV DHE and placebo on pulmonary artery pressure.



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Pharmacokinetics (PK) trial: This completed trial showed that the systemic absorption of LEVADEX was not higher and systemic exposure to DHE was not greater in smokers than in non-smokers. This single dose, open-label, crossover trial compared the PK of LEVADEX to IV DHE in both smokers and non-smokers.

We hold worldwide commercialization rights for LEVADEX and our goal is to market LEVADEX in the United States through our own focused sales force targeting neurologists and headache specialists. We may establish partnerships with pharmaceutical companies to market and sell to primary care physicians and specialists both inside and outside of the United States.

MAP Pharmaceuticals, Inc., incorporated in the state of Delaware, was originally formed as a limited liability company on July 3, 2003 and converted to a corporation on December 11, 2003. Our principal executive offices are located at 2400 Bayshore Parkway, Suite 200, Mountain View, CA 94043, and our telephone number at that address is (650) 386-3100. Our website can be found at [www.mappharma.com](http://www.mappharma.com). The information contained in, or that can be accessed through, our website is not part of this prospectus supplement or any accompanying prospectus supplement.

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**The Offering**

The following summary is qualified in its entirety by reference to the more detailed information appearing elsewhere in this prospectus supplement. For more information concerning our common stock, see Description of Common Stock.

Issuer	MAP Pharmaceuticals, Inc.
The Nasdaq Global Market Symbol	MAPP
Common Stock Offered by us	3,000,000 shares (or 3,450,000 shares if the underwriters exercise in full their over-allotment option to purchase additional shares)
Common Stock to be Outstanding Immediately After this Offering (1)	29,674,034 shares (or 30,124,034 shares if the underwriters exercise in full their over-allotment option to purchase additional shares)
Risk Factors	See Risk Factors beginning on page S-5 of this prospectus supplement and on page 1 of the accompanying prospectus for a discussion of the factors you should carefully consider before deciding to invest in our common stock.
Use of Proceeds	We estimate that the net proceeds from this offering, after deducting underwriting discounts and commissions and before estimated offering expenses, will be approximately \$41.3 million (or approximately \$47.5 million if the underwriters exercise in full their over-allotment option to purchase additional shares), based on the offering price of \$14.50 per share. We intend to apply the net proceeds from this offering for general corporate purposes, focusing on clinical development of LEVADEX. For more information, see Use of Proceeds.
Certain Material United States Federal Income Tax Consequences to Non-U.S. Holders	You should consult with your tax advisor with respect to the U.S. federal income tax considerations of owning our common stock in light of your own particular situation and with respect to any tax considerations arising under the laws of any state, local, foreign or other taxing jurisdiction. See Certain Material United States Federal Income Tax Consequences to Non-U.S. Holders.

(1) The number of shares of our common stock to be outstanding immediately after this offering as shown above is based on shares outstanding as of September 28, 2010. This number excludes 4,033,889 shares of common stock issuable upon the exercise of outstanding stock options, and warrants to purchase shares of our common stock, 98,000 performance-based restricted stock units and 450,000 shares subject to the underwriters' over-allotment option.



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**FORWARD-LOOKING STATEMENTS**

All statements included or incorporated by reference into this prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement, other than statements of historical facts, that address activities, events or developments that we intend, expect, project, believe or anticipate will or may occur in the future are forward looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the "safe harbor" created by those sections. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement contain forward looking statements that are based on current expectations, estimates, forecasts and projections about us, our future performance, our business or others on our behalf, our beliefs and our management's assumptions. In some cases you can identify forward-looking statements by words such as may, will, should, could, would, expects, plan, anticipates, believes, estimates, projects, predicts, potential and similar expressions intended to identify forward-looking statements. Examples of these statements include, but are not limited to, statements regarding:

governmental regulation and approval;

the implications of interim or final results of our clinical trials, the progress of our research programs, including clinical testing;

the extent to which our issued and pending patents may protect our products and technology;

our ability to identify new product candidates;

the potential of such product candidates to lead to the development of commercial products;

our anticipated timing for initiation or completion of our clinical trials for any of our product candidates;

our future operating expenses;

our future losses;

our future expenditures for research and development; and

the sufficiency of our cash resources.

Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including the risks faced by us and described in "Risk Factors" elsewhere in this prospectus supplement. You should not place undue reliance on these forward-looking statements, which apply only as of the date of this prospectus supplement. These cautionary statements should be considered in connection with any written or oral forward looking statements that we may issue in the future. Except as required by law, we assume no obligation to update these forward-looking statements, whether as a result of new information, future events or otherwise.



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**RISK FACTORS**

*An investment in our common stock involves a high degree of risk. You should carefully consider the following risk factors in addition to the remainder of this prospectus supplement and the accompanying prospectus, including the information incorporated by reference, before making an investment decision. In addition, you should carefully consider, among other things, the matters discussed under Risk Factors in our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2010, and in other documents that we subsequently file with the SEC, all of which are incorporated by reference into this prospectus supplement and the accompanying prospectus. The risks and uncertainties described in such incorporated documents and described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. If any of those risks actually occurs, our business, financial condition and results of operations would suffer. In that event, the trading price of our common stock could decline, and you may lose all or part of your investment in our common stock. The risks discussed below also include forward-looking statements and our actual results may differ substantially from those discussed in these forward-looking statements. See Forward-Looking Statements.*

**Risks Relating to Our Financial Position and Need for Additional Capital**

We have a history of net losses. Currently, we have no products approved for commercial sale, and to date we have not generated any product revenue. As a result, we expect to continue to incur substantial and increasing net losses for the foreseeable future, and we may never achieve or maintain profitability.

We are not profitable and do not expect to be profitable in the foreseeable future. We have incurred significant net losses and negative cash flow in each year since our inception, including net losses of approximately \$40.1 million, \$72.9 million and \$9.0 million, for the years ended December 31, 2007, 2008 and 2009, respectively and \$12.5 million and \$26.5 million for the quarter and six months ended June 30, 2010, respectively. As of June 30, 2010, we had a deficit accumulated during development stage of approximately \$211.4 million. We have devoted most of our financial resources to research and development, including our pre-clinical development activities and clinical trials. We have not completed development of, or commercialized any product candidate and have therefore not generated any product revenues. In that regard, we expect to have substantial expenses as we continue with our Phase 3 clinical program for LEVADEX, our most advanced product candidate, and conduct other clinical trials. In addition, if we are required by the U.S. Food and Drug Administration, or the FDA, to perform studies in addition to those we currently anticipate, our expenses will increase beyond expectations and the timing of any potential product approval may be delayed. We also expect an increase in our expenses associated with our manufacturing work and with preparing for commercialization. In addition, we expect to continue to incur costs to support operations as a public company. As a result, we may continue to incur substantial net losses and negative cash flow for the foreseeable future. These losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of substantial expenses or when, or if, we will be able to achieve or maintain profitability. We have financed our operations primarily through the sale of equity securities, collaboration payments and debt financings. The size of our future net losses will depend, in part, on the rate of growth of our expenses and the rate of growth, if any, of our revenues. Revenues from potential strategic partnerships are uncertain because we may not enter into any additional strategic partnerships. On July 8, 2009, we received a notice of termination of our license agreement with AstraZeneca AB, or the AstraZeneca Agreement, related to our Unit Dose Budesonide, or UDB, product candidate. Under the AstraZeneca Agreement, AstraZeneca had agreed to fund our remaining development activities for UDB and to reimburse us for costs we incur with respect to future development activities conducted for the U.S. registration of our UDB product candidate, subject to the terms and conditions of the AstraZeneca Agreement. Following the termination of the AstraZeneca Agreement, we suspended development of UDB. If we are unable to develop and commercialize our other product candidates, including pursuant to strategic partnerships, or if sales revenue from any product candidate that receives marketing approval is insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability.

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**We have a limited operating history, and we expect a number of factors to cause our operating results to fluctuate on a quarterly and annual basis, which may make it difficult to predict our future performance.**

Our operations to date have been primarily limited to organizing and staffing our company, developing our technology and undertaking pre-clinical studies and clinical trials of our product candidates. We have not yet obtained regulatory approvals for any of our product candidates. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history. Specifically, our financial condition and operating results have varied significantly in the past and will continue to fluctuate from quarter-to-quarter and year-to-year in the future due to a variety of factors, many of which are beyond our control. Factors relating to our business that may contribute to these fluctuations include the following factors, among others:

our ability to obtain additional funding to develop our product candidates;

the need to obtain regulatory approval of our most advanced product candidate, LEVADEX for the potential treatment of migraine;

potential risks related to any collaborations we may enter into for our product candidates, including LEVADEX;

delays in the commencement, enrollment and completion of clinical testing, as well as the analysis and reporting of results from such clinical testing;

the success of clinical trials of our LEVADEX product candidate or future product candidates;

any delays in regulatory review and approval of product candidates in development;

our ability to receive regulatory approval or commercialize our product candidates;

our ability to rely on Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FFDC, to seek FDA marketing approval of our product candidates;

market acceptance of our product candidates for which we obtain regulatory approval;

our ability, and our partners' ability, to establish an effective sales and marketing infrastructure;

competition from existing products or new products that may emerge;

the impact of competition, including generics, in the migraine market on our ability to commercialize LEVADEX;

the ability of patients to obtain coverage of or sufficient reimbursement for our products;

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the ability to receive regulatory approval or commercialize our products outside of the United States;

potential side effects of our future products that could delay or prevent commercialization or cause an approved drug to be taken off the market;

regulatory difficulties relating to products that have already received regulatory approval;

guidelines and recommendations of therapies published by various organizations;

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potential product liability claims;

potential liabilities associated with hazardous materials;

our ability to maintain adequate insurance policies;

our dependency on third-party manufacturers to supply or manufacture our products;

our ability to establish or maintain collaborations, licensing or other arrangements;

our ability, our partners' abilities, and third parties' abilities to protect and assert intellectual property rights;

costs related to and outcomes of potential intellectual property litigation;

compliance with obligations under intellectual property licenses with third parties;

our ability to adequately support future growth; and

our ability to attract and retain key personnel to manage our business effectively.

Due to the various factors mentioned above, and others, the results of any prior quarterly or annual periods should not be relied upon as indications of our future operating performance.

**We will need substantial additional funding and if we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs.**

Developing biopharmaceutical products, including conducting pre-clinical studies and clinical trials and establishing manufacturing capabilities, is expensive. We expect to have substantial research and development expenses in connection with our ongoing activities, particularly as we focus on and proceed with our Phase 3 clinical program of LEVADEX, our most advanced product candidate. In addition, our expenses could increase beyond expectations if the FDA requires that we perform additional studies to those that we currently anticipate, in which case the timing of any potential product approval may be delayed. We believe that our existing cash and cash equivalents will be sufficient to fund our projected operating requirements for at least 12 months. We will need substantial additional capital in the future in order to complete the development and commercialization of LEVADEX and to fund the development and commercialization of future product candidates. Until we can generate a sufficient amount of product revenue, if ever, we expect to finance future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements. Such funding, if needed, may not be available on favorable terms, if at all. In the event we are unable to obtain additional capital, we may delay or reduce the scope of our current research and development programs and other expenses

If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our research or development programs or our commercialization efforts. To the extent that we raise additional funds by issuing equity securities, our stockholders may experience additional significant dilution, and debt financing, if available, may involve restrictive covenants. To the extent that we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish some rights to our technologies or our product candidates or to grant licenses on terms that may not be favorable to us. We may seek to access the public or private capital markets whenever conditions are favorable, even if we do not have an immediate need for additional capital at that time.

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Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this Risk Factors section. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements will depend on many factors, including, but not limited to:

the scope, rate of progress and cost of our clinical trials and other research and development activities;

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the costs and timing of regulatory approval;

the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;

the effect of competing technological and market developments;

the terms and timing of any collaboration, licensing or other arrangements that we may establish;

the cost and timing of completion of clinical and commercial-scale manufacturing activities; and

the costs of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval.

**Risks Relating to the Development, Regulatory Approval and**

**Commercialization of Our Product Candidates**

**We are largely dependent on the success of one product candidate, and we cannot be certain that this product candidate will receive regulatory approval.**

We have invested a significant portion of our efforts and financial resources in the development of LEVADEX and UDB. In February 2009, we announced top-line results from our first Phase 3 trial of UDB, indicating that the trial did not meet its co-primary endpoints in either dose evaluated when compared to placebo. In July 2009, we announced that we were suspending development of UDB, after our partner AstraZeneca terminated our license agreement. We are now largely dependent on the success of one product candidate, LEVADEX, for which we are conducting a Phase 3 clinical development program. Our ability to generate product revenue, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful development, regulatory approval and commercialization of this product candidate. We may have inadequate financial or other resources to advance LEVADEX through the clinical trial process, depending on the requirements of the FDA. In May 2009, we announced top-line results from the efficacy portion of our first Phase 3 trial of LEVADEX, indicating that the trial met all its co-primary endpoints when LEVADEX was compared to placebo. A long-term safety extension of the trial is ongoing. Although we had planned to initiate a second Phase 3 efficacy study in the first quarter of 2010, we have been informed by the FDA that a second pivotal efficacy study is not required for submission of our NDA if the topline efficacy results we submitted in 2009 are confirmed during the NDA review. We have completed a pharmacokinetics trial in 23 adult smokers comparing them to 24 adult non-smokers. The trial was designed to measure whether the systemic absorption of LEVADEX is higher and exposure to dihydroergotamine mesylate, or DHE, is greater in smokers than in non-smokers. In the trial, the systemic absorption of LEVADEX was not higher and systemic exposure to DHE was not greater in smokers than in non-smokers. We also have completed a pharmacodynamics trial evaluating pulmonary artery pressure in approximately 24 healthy volunteers using echocardiograms. The trial compared the acute effects on pulmonary artery pressure of LEVADEX, DHE administered intravenously and placebo. In the trial, there was no statistically significant difference between the LEVADEX and placebo groups in the primary endpoint of pulmonary artery pressure over two hours after administration. In addition we have completed patient treatment in a thorough QT trial evaluating whether LEVADEX has an effect on QT interval as measured by electrocardiograms in support of our application to the FDA for regulatory approval. We expect treatment in our remaining LEVADEX clinical trials to be completed in 2010. Our clinical development program for LEVADEX may not lead to regulatory approval from the FDA and similar foreign regulatory agencies if we fail to demonstrate that the product candidate is safe and effective in our planned clinical trials, and we may therefore fail to commercialize LEVADEX. Any failure to obtain regulatory approval of LEVADEX would have a material and adverse impact on our business.



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With the suspension of development for our UDB product candidate, LEVADEX is our only current product candidate in late stage development. Our drug development efforts may not produce any other proprietary product candidates. We cannot be certain that we will be able to acquire or in-license other product candidates or develop a next generation budesonide therapy for the treatment of asthma in children, should we pursue these activities. Our failure to develop product candidates will limit our ability to generate additional revenue.

We currently have no approved drug products for sale and we cannot guarantee that we will ever have marketable drug products. The research, testing, manufacturing, labeling, approval, selling, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, with regulations differing from country to country. We are not permitted to market our product candidates in the United States until we receive approval of an NDA from the FDA for each product candidate. We have not submitted an NDA or received marketing approval for any of our product candidates. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. Markets outside of the United States also have requirements for approval of drug candidates which we must comply with prior to marketing.

**We may enter into collaborations with third parties to develop and commercialize our product candidates, including LEVADEX. These collaborations may place the development of our product candidates outside our control, may require us to relinquish important rights or may otherwise be on terms unfavorable to us.**

We may enter into collaborations with third parties to develop and commercialize our product candidates, including LEVADEX. Our dependence on future partners for development and commercialization of our product candidates will subject us to a number of risks, including:

we may not be able to control the amount and timing of resources that our partners may devote to the development or commercialization of product candidates or to their marketing and distribution;

partners may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

disputes may arise between us and our partners that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management's attention and resources;

partners may experience financial difficulties;

partners may not properly maintain or defend our intellectual property rights, or may use our proprietary information, in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or proprietary information or expose us to potential litigation;

business combinations or significant changes in a partner's business strategy may adversely affect a partner's willingness or ability to meet its obligations under any arrangement;

a partner could independently move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors; and

the collaborations with our partners may be terminated or allowed to expire, which would delay the development and may increase the cost of developing our product candidates.



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### **Delays in the commencement, enrollment and completion of clinical testing could result in increased costs to us and delay or limit our ability to obtain regulatory approval for our product candidates.**

Delays in the commencement, enrollment and completion of clinical testing could significantly affect our product development costs. We do not know whether planned clinical trials for LEVADEX will be completed on schedule, if at all. The commencement and completion of clinical trials requires us to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs for the same indication as our product candidates or may be required to withdraw from our clinical trial as a result of changing standards of care or may become ineligible to participate in clinical studies. The commencement, enrollment and completion of clinical trials can be delayed for a variety of other reasons, including delays related to:

reaching agreements on acceptable terms with prospective contract research organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

obtaining regulatory approval to commence a clinical trial;

obtaining institutional review board, or IRB, approval to conduct a clinical trial at numerous prospective sites;

recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including meeting the enrollment criteria for our study and competition from other clinical trial programs for the same indication as our product candidates;

retaining patients who have initiated a clinical trial but may be prone to withdraw due to the treatment protocol, lack of efficacy, personal issues or side effects from the therapy or who are lost to further follow-up;

maintaining and supplying clinical trial material on a timely basis; and

collecting, analyzing and reporting final data from the clinical trials.

In addition, a clinical trial may be suspended or terminated by us, the FDA or other regulatory authorities due to a number of factors, including:

failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;

inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;

unforeseen safety issues or any determination that a trial presents unacceptable health risks; and

lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties.

We are conducting a Phase 3 clinical program to support our NDA for LEVADEX. In October 2009, we submitted our topline efficacy results for the double-blind efficacy portion of our pivotal Phase 3 study. We recently completed a pharmacokinetics trial in healthy adult smokers and

non-smokers and a pharmacodynamics trial measuring pulmonary artery pressure in healthy adults. We are currently completing the long-term safety extension of our pivotal Phase 3 trial and have completed treatment in a thorough QT trial in support of our NDA for LEVADEX. FDA communicated its agreement with the design, execution, and analyses for our pivotal Phase 3 trial, which we submitted to the Agency under the Special Protocol Assessment, or SPA, process and modified as suggested by FDA. Under a SPA, the FDA agrees to not later alter its position with respect to adequacy of the design, execution, or analyses of the clinical trial intended to form the primary basis of an effectiveness claim in an NDA, without the sponsor's agreement unless the FDA identifies a substantial scientific issue essential to determining the safety or efficacy of the drug after testing begins. In March 2010, we held a pre-NDA meeting with the FDA to discuss the clinical portion of our anticipated NDA filing. The FDA's minutes of that meeting state that, while the FDA did not have a record of a formal SPA, the FDA concurred with the selection of our co-primary endpoints and confirmed that a second pivotal efficacy study was not necessary if topline efficacy results were confirmed during the NDA review. We believe that our prior written correspondence and interactions with the FDA under the SPA process constitute an SPA with the agency. The FDA may take a different view and could request additional safety and efficacy studies without having to identify a substantial scientific issue with our Phase 3 trial that is essential to determining the safety and efficacy of LEVADEX. If we are required to conduct additional clinical trials or other testing of our LEVADEX product candidate beyond those that we currently contemplate, we may be delayed in obtaining, or may not be able to obtain, marketing approval for this product candidate. We may not be able to obtain approval for indications that are as broad as intended or we may obtain approval for indications different than those indications for which we seek approval. Furthermore we may not be able to obtain approval for any of our other product candidates.

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Additionally, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes with appropriate regulatory authorities. Amendments may require us to resubmit our clinical trial protocols to IRBs for re-examination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in the completion of, or if we terminate, our clinical trials, the commercial prospects for our product candidates will be harmed, and our ability to generate product revenues will be delayed. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Even if we are able to ultimately commercialize our product candidates, other therapies for the same or similar indications may have been introduced to the market and established a competitive advantage.

**Because the results of prior clinical trials are not necessarily predictive of future results, LEVADEX or any other product candidate advanced into clinical trials may not have favorable results in subsequent clinical trials or receive regulatory approval.**

Success in pre-clinical studies and clinical trials does not ensure that subsequent clinical trials will generate adequate data to demonstrate the efficacy and safety of the investigational drug. A number of companies in the pharmaceutical industry, including those with greater resources and experience, have suffered significant setbacks in Phase 3 clinical trials, even after seeing promising results in prior clinical trials.

In May 2009, we announced top-line results from the efficacy portion of our Phase 3 trial of LEVADEX, indicating that the trial met all four of its co-primary endpoints when LEVADEX was compared to placebo. A long-term safety extension of this Phase 3 trial is ongoing, and we expect to complete patient treatment by the end of the year. In July 2010, we announced that in a pharmacokinetics trial of LEVADEX, systemic absorption of LEVADEX was not higher and systemic exposure to DHE was not greater in smokers than in non-smokers. In September 2010, we reported results from a pharmacodynamics trial comparing the acute effects on pulmonary artery pressure of LEVADEX, DHE administered intravenously and placebo. In the trial, there was no statistically significant difference between the LEVADEX and placebo groups in the primary endpoint of pulmonary artery pressure over two hours after administration. We also announced that we completed patient treatment in a thorough QT trial. In order to obtain regulatory approval for LEVADEX, we need to complete the long-term safety extension trial and the analysis of the results of the thorough QT trial. The data collected from our clinical trials may not be adequate to support regulatory approval of LEVADEX or any of our other product candidates. Even if we obtain regulatory approval of a product candidate, the FDA may require continuing evaluation and study of our product through clinical trials as a condition of any approval. Despite the results reported in prior clinical trials for our product candidates, we do not know whether subsequent clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market our product candidates. For example, after receiving positive data from a previous Phase 2 trial, in February 2009 we announced top-line results from our Phase 3 trial of UDB, indicating that the trial did not meet its co-primary endpoints in either dose evaluated when compared to placebo.

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**If clinical trials of our LEVADEX product candidate or future product candidates do not produce results necessary to support regulatory approval in the United States or elsewhere or show undesirable side effects, we will be unable to commercialize these products.**

To receive regulatory approval for the commercial sale of LEVADEX or any other product candidates, we must conduct adequate and well-controlled clinical trials to demonstrate efficacy and safety in humans. Clinical testing is expensive, takes many years and has an uncertain outcome. Clinical failure can occur at any stage of the testing. Our clinical trials may produce negative or inconclusive results. In such cases, we may decide, or regulators may require us, to conduct additional clinical and/or non-clinical testing, or we may decide not to pursue further development of a product candidate, such as the case of our UDB product candidate, where top-line results of our Phase 3 clinical trial indicated that the trial failed to meet the primary endpoints. Subsequently we suspended development of UDB. In addition, the results of our clinical trials may show that our product candidates may cause undesirable side effects, which could interrupt, delay or halt clinical trials, resulting in our inability to obtain regulatory approval by the FDA and other regulatory authorities.

In light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of Congress, the Government Accounting Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials and regulatory approval. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense and a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

Our failure to adequately demonstrate the efficacy and safety of LEVADEX or any other product candidates would prevent regulatory approval and, ultimately, the commercialization of that product candidate.

**All of our product candidates in development require regulatory review and approval prior to commercialization. Any delay in the regulatory review or approval of any of our product candidates in development will harm our business.**

All of our product candidates in development require regulatory review and approval prior to commercialization. Any delays in the regulatory review or approval of our product candidates in development would delay market launch, increase our cash requirements and result in additional operating losses.

The process of obtaining FDA and other required regulatory approvals, including foreign approvals, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved. Furthermore, this approval process is extremely complex, expensive and uncertain. We or our partners may not be able to maintain our proposed schedules for the submission of any NDA in the United States or any marketing approval application or other foreign applications for any of our products. If we or our partners submit any NDA, including any amended NDA or supplemental NDA, to the FDA seeking marketing approval for any of our product candidates, the FDA must decide whether to either accept or reject the submission for filing. We cannot be certain that any of these submissions will be accepted for filing and reviewed by the FDA, or that our marketing approval application submissions to any other regulatory authorities will be accepted for filing and review by those authorities. We cannot be certain that we or our partners will be able to respond to any regulatory requests during the review period in a timely manner without delaying potential regulatory action. We also cannot be certain that any of our product candidates will receive favorable recommendation from any FDA advisory committee or foreign regulatory bodies or be approved for marketing by the FDA or foreign regulatory authorities. In addition, delays in approvals or rejections of marketing applications may be based upon many factors, including regulatory requests for additional analyses, reports, data and/or studies, regulatory questions regarding data and results, changes in regulatory policy during the period of product development and/or the emergence of new information regarding our products or other products.

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Data obtained from pre-clinical studies and clinical trials are subject to different interpretations, which could delay, limit or prevent regulatory review or approval of any of our products. In addition, as a routine part of the evaluation of any potential drug, clinical studies are generally conducted to assess the potential for drug drug interactions that could impact potential product safety. At this point in time, we have not been requested to perform drug drug interaction studies, but any such requirement may delay any potential product approval and will increase our expenses associated with our clinical programs. Furthermore, regulatory attitudes towards the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects.

In addition, the environment in which our regulatory submissions may be reviewed changes over time. For example, average review times at the FDA for marketing approval applications have fluctuated over the last ten years, and we cannot predict the review time for any of our submissions with any regulatory authorities. In addition, review times can be affected by a variety of factors, including budget and funding levels and statutory, regulatory and policy changes.

**We may not be able to rely on Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, which could result in a longer development program and more costly trials than we anticipate.**

We may not be able to seek FDA marketing approval of our product candidates under Section 505(b)(2) of the FFDCA. Section 505(b)(2), if applicable to us, would allow an NDA we file with the FDA to rely in part on data in the public domain or the FDA's prior conclusions regarding the safety and effectiveness of approved compounds, which could expedite the development program for our product candidates by potentially decreasing the overall scope of work we must do ourselves. If we are unable to rely on Section 505(b)(2), the development program for our product candidates would be longer than we expect, and we would also have to conduct more costly trials than we anticipate.

**If any of our product candidates for which we or our partners receive regulatory approval do not achieve broad market acceptance, the revenues that we generate from their sales will be limited.**

The commercial success of our product candidates for which we or our partners obtain marketing approval from the FDA or other regulatory authorities will depend upon the acceptance of these products among physicians, the medical community, patients, and coverage and reimbursement of them by third-party payors, including government payors. The degree of market acceptance of any of our approved products will depend on a number of factors, including:

a product's FDA-approved labeling as well as limitations or warnings contained in the labeling;

changes in the standard of care for the targeted indications for any of our product candidates, which could reduce the marketing impact of any claims that we could make following FDA approval;

limitations inherent in the approved indication for any of our product candidates compared to more commonly understood or addressed medical conditions;

lower demonstrated efficacy and a less favorable safety or tolerability profile compared to other products;

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device-related difficulties associated with our Tempo inhaler;

prevalence and severity of adverse effects;

ineffective marketing and distribution efforts;

lack of availability of reimbursement from managed care plans and other third-party payors;

lack of cost-effectiveness;

timing of market introduction and perceived effectiveness of competitive products;