MAP Pharmaceuticals, Inc.
Form 10-K
March 04, 2011
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2010

OR

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from _____ to _____

Commission File Number 001-33719

MAP PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**20-0507047**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

2400 Bayshore Parkway, Suite 200

Mountain View, California	**94043**
(Address of principal executive offices)	**(Zip code)**

(650) 386-3100

(Registrant s telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock per share $0.01 par value	**The NASDAQ Global Market**

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ¨ No x

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ¨ No ¨

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

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

Large accelerated filer ¨	Accelerated filer x
Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined by Rule 12b-2 of the Exchange Act). Yes ¨ No x

The aggregate market value of the voting and non-voting common equity stock held by non-affiliates of the registrant was $181,594,769 as of June 30, 2010, the last day of the registrant s second fiscal quarter during its fiscal year ended December 31, 2010, based upon the closing sale price on The NASDAQ Global Market reported for such date. Shares of Common Stock held by each officer and director and by each person who may be deemed to be an affiliate have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 28, 2011, the registrant had outstanding 30,204,049 shares of Common Stock.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s proxy statement to be filed with the Securities and Exchange Commission, or the SEC, pursuant to Regulation 14A in connection with the registrant s 2011 Annual Meeting of Stockholders, to be filed subsequent to the date hereof, are incorporated by reference into Part III of this Annual Report on Form 10-K. Such proxy statement will be filed with the SEC not later than 120 days after the conclusion of the registrant s fiscal year ended December 31, 2010.

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PART I

ITEM 1. BUSINESS

Overview

Our goal is to use our proprietary inhalation technologies to enhance the therapeutic benefits and commercial attractiveness of proven drugs in the field of neurology 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.

Our strategy is to commercialize and develop differentiated neurology product candidates that can address significant unmet medical needs and overcome limitations of existing products. Key elements of our strategy include:

- Obtain regulatory approval for our most advanced product candidate, LEVADEX orally inhaled migraine therapy, for the potential acute treatment of migraine;
- Build a specialized sales force to commercialize LEVADEX to neurologists and pain specialists in the United States;
- Expand the market opportunity for LEVADEX; and
- Advance and expand our neurology product pipeline by leveraging our technologies and our extensive scientific expertise in aerosol science and medicine to develop additional potential product candidates offering unique features and benefits.

Our current focus is to advance our lead product candidate, LEVADEX (MAP0004) orally inhaled migraine therapy, a proprietary orally inhaled version of dihydroergotamine mesylate, or DHE, for the potential acute treatment of migraine. We completed clinical development for LEVADEX in 2010 and we plan to submit a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, in the first half of 2011. In collaboration with Allergan, Inc., we plan to commercialize LEVADEX directly to neurologists and pain specialists in the United States. We are also evaluating options to commercialize LEVADEX to primary care physicians in the United States and to physicians in markets outside the United States.

Our Lead Product Candidate

Migraine is a chronic and debilitating neurological disorder characterized by episodic attacks. Migraine attacks typically manifest themselves as moderate to severe headache pain, with associated symptoms that often include nausea and vomiting, photophobia, phonophobia, and visual disturbances or aura. They usually involve pounding or throbbing pain on one side of the head, although pain may occur on both sides. Migraines limit the normal functioning of patients, who often seek dark, quiet surroundings until the episode has passed. Most migraines last between four and 24 hours, but some last as long as three days. According to published studies, the median frequency of attack is 1.5 times per month, although approximately 25% of migraine sufferers experience one or more attacks every week.

Migraine is a major public health problem that affects up to approximately 12% of the population in the United States and approximately 15% in Europe. According to the National Headache Foundation, approximately 30 million people in the United States suffer from migraine. Migraine is more common in women, with about 18% of women affected and 6% of men. Migraine prevalence is highest during the peak productive ages of 25 to 55, which results in high costs to employers and managed care organizations.

Migraine is listed in the top 20 causes of disabling conditions and in the top four neurologic disabling conditions by the World Health Organization (WHO). Related disability from migraine is substantial, with over 90% of sufferers experiencing functional impairment with their migraine that can disrupt every aspect of day to

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day life, including work, school, family and social relationships. More than half of the sufferers report severe impairment or the need for bed rest as a result of their migraines, according to published surveys. The economic burden of migraine remains substantial despite existing treatments with migraine patients losing four to six work days each year due to headache. The combination of direct and indirect costs of migraine in the United States is estimated at over $20 billion annually.

In 2008, according to market data, approximately 29 million prescriptions were written for the treatment of migraine in the United States. Approximately 12 million of those prescriptions were written for acute migraine specific drugs. The majority of acute migraine specific drug prescriptions written were in the triptan class. In 2010, the triptan market in the United States totaled approximately $1.6 billion in revenues.

We have designed LEVADEX to provide faster onset and longer-lasting migraine relief than triptans, the class of drugs most often prescribed for treating migraine. LEVADEX is an easy to use, at-home therapy in development that patients self-administer using our proprietary hand-held TEMPO® inhaler. DHE currently is available as an intravenous, or IV, therapy which has been used in clinical settings for over 50 years for the safe and effective treatment of migraine, particularly forms of migraine that are severe or do not respond to triptans or other therapies. We believe LEVADEX has the potential to be suitable as a first-line therapy for some migraine patients.

In May 2009, we announced results of the efficacy portion of our Phase 3 clinical trial of LEVADEX, or FREEDOM-301. We announced that the clinical trial met its four primary endpoints, pain relief and being phonophobia, photophobia and nausea 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.

Patients taking LEVADEX therapy had statistically significant improvement at two hours compared to patients on placebo for each of the primary endpoints:

- Pain relief: 58.7% of patients who received LEVADEX compared with 34.5% for placebo ($p<0.0001$);
- Phonophobia free: 52.9% of patients who received LEVADEX compared with 33.8% for placebo ($p<0.0001$);
- Photophobia free: 46.6% of patients who received LEVADEX compared with 27.2% for placebo ($p<0.0001$); and
- Nausea free: 67.1% of patients who received LEVADEX compared with 58.7% for placebo ($p=0.02$).

A total of 792 patients were included in the primary data analysis as specified in the protocol of the FREEDOM-301 study. The patient population studied had more severe migraine pain than anticipated, with 46% reporting severe pain and 54% reporting moderate pain prior to administration of the study drug.

Results from additional pre-defined analyses include:

- LEVADEX therapy achieved statistically significant onset of pain relief at 30 minutes after dosing ($p=0.03$);
- While not statistically significant, 50% more of the patients receiving LEVADEX therapy than the patients receiving placebo reported pain relief at 10 minutes;
- LEVADEX therapy achieved statistically significant sustained pain relief from two to 24 hours ($p<0.0001$), as well as two to 48 hours ($p<0.0001$, when unadjusted for multiplicity);

LEVADEX therapy achieved statistically significant pain freedom (pain symptom score = 0) as early as 30 minutes (p=0.002, when unadjusted for multiplicity); and

LEVADEX therapy achieved sustained pain freedom from two to 24 hours, as well as two to 48 hours (p<0.0001 for both time points, when unadjusted for multiplicity).

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LEVADEX was well tolerated, with the most common adverse event reported being medication aftertaste at 6%, with 2% of patients receiving placebo also reporting medication aftertaste. The next most common adverse event was nausea at 5%, compared with 2% for placebo. Symptoms or sensitivities typically associated with commonly used triptan migraine treatments, such as chest discomfort (1%) or chest pain (0%), were rare and comparable to placebo. There were no mean decreases in lung function, as measured by spirometry, between the active and placebo groups. There were no drug-related serious adverse events reported in the trial. These data were presented in September 2009 in a late-breaking session of the 14th Congress of the International Headache Society.

In 2010, we announced that a second Phase 3 clinical trial would not be required for the LEVADEX NDA submission, completed and announced successful results from a pharmacokinetic (PK) trial in smokers, a pharmacodynamics (PD) trial evaluating pulmonary artery pressure using echocardiogram and a thorough QT trial. In addition, we completed our 12 month open-label safety extension of the Phase 3 FREEDOM 301 trial. In our clinical trials conducted for LEVADEX, no drug related serious adverse events have been reported. The LEVADEX clinical development program evaluated the efficacy, safety, PK and PD of LEVADEX in approximately 1,000 patients. We plan to submit an NDA to the FDA in the first half of 2011.

On January 28, 2011 we entered into a Collaboration Agreement and Co-Promotion Agreement with Allergan, Inc., Allergan USA, Inc. and Allergan Sales, LLC (collectively, Allergan) to promote LEVADEX to neurologists and pain specialists within the United States. Under the terms of these agreements, following potential FDA approval, together with Allergan, we will co-promote LEVADEX to neurologists and pain specialists in the United States. Specifically, Allergan will leverage its existing U.S. sales force dedicated to headache specialists using BOTOX® for Chronic Migraine, which will be complemented by our field sales force targeting neurologists and pain specialists. If LEVADEX receives FDA approval, profits and losses from sales of LEVADEX generated from commercialization to neurologists and pain specialists in the United States will be shared equally between us and Allergan. Following potential approval of LEVADEX for the acute treatment of migraine in adults, we and Allergan will equally share regulatory, patent and development expenses for two future LEVADEX indications. We retain all rights to commercialize LEVADEX outside the United States, subject to Allergan s right under certain circumstances to expand the territory in which the parties will commercialize LEVADEX to neurologists and pain specialists to include Canada, and we retain all rights to commercialize LEVADEX to other physicians, including primary care physicians within the United States.

As part of the collaboration, we will be responsible for the manufacturing and distribution of LEVADEX in the United States, and for recording product revenues. The companies also have agreed, following potential approval of LEVADEX for the treatment of acute migraine in adults, to jointly develop LEVADEX for the treatment of migraine in adolescents 12 to 18 years of age and for one other additional indication. We are responsible for obtaining NDA approval, and will retain ownership of the NDA.

In February 2011, we received a $60.0 million up-front payment from Allergan and may receive up to $97 million in the form of regulatory milestones, including milestones for acceptance of filing of the LEVADEX NDA and first commercial sale associated with the initial acute migraine indication.

We may establish other partnerships with pharmaceutical companies to market LEVADEX outside the United States and to primary care physicians in the United States.

Other Product Technologies

We are exploring options to advance and expand our neurology product pipeline by leveraging our technologies and our extensive scientific expertise in aerosol science and medicine to develop additional neurological product candidates offering unique features and benefits.

Nebulized Corticosteroid Particle Technology: We have expertise in the formulation and administration of nebulized corticosteroids for the treatment of pediatric asthma. We have created novel versions of budesonide

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that are designed to be administered more quickly and to provide efficacy at lower doses than conventional nebulized budesonide. Conventional nebulized budesonide is an inhaled corticosteroid approved by the FDA for treating asthma in children from 12 months up to eight years of age. We have developed novel morphologies of corticosteroid particles which may allow for faster delivery and efficacy at a lower dose, which together may offer improved safety, compliance and convenience.

Combination Particle Technology: We have applied our proprietary particle formulation technologies to deliver the optimal ratio of multiple drugs in a reproducible and consistent manner. We can combine two or more drugs together into a single micron scale inhalable particle at consistent and reproducible ratios, which may improve the delivery profile and stability of the resultant combination therapy. We believe our proprietary technologies in this area have potential broad applicability for a number of combination product candidates in diverse indications via inhalation and other routes of delivery.

Stable Protein & Peptide Technology: We have also demonstrated our ability to apply our proprietary technologies to formulate and stabilize biologically active proteins and peptides. We design and incorporate our protein formulations without the need for excipients or other additives, to be stored for months at room temperature and to provide multiple doses of medicine delivered accurately without the need for needle injections.

A component of our strategy is to reduce the risk of drug development by focusing on the development of proven drugs with established safety and efficacy profiles. The compounds underlying our product candidates are well characterized and have been previously approved by the FDA or foreign agencies for other sponsors and in other dosage forms and formulations. As a result, we may seek FDA marketing approval of our product candidates under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FFDCA, which, if available to us, would allow any 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. This may expedite the development program for our product candidates by potentially decreasing the overall scope of work we must do ourselves.

Information About our Development Programs

LEVADEX for the Acute Treatment of Migraine

LEVADEX is our proprietary orally inhaled version of DHE that has completed Phase 3 clinical development for the acute treatment of migraine, a syndrome characterized by four symptoms: pain, nausea, phonophobia, or abnormal sensitivity to sound, and photophobia, or abnormal sensitivity to light. LEVADEX is an easy to use, non-invasive, at-home therapy in development that patients self-administer using our proprietary handheld TEMPO inhaler. DHE is available as an IV therapy which has been used in clinical settings for over 50 years for the safe and effective treatment of migraine, particularly forms of migraine that are severe or do not respond to triptans or other therapies. We believe DHE s adoption as a first-line therapy has been limited by its invasive mode of administration and high incidence of nausea.

In May 2009, we announced results from the efficacy portion of our completed Phase 3 clinical trial of LEVADEX, or FREEDOM-301. 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. LEVADEX was well tolerated and there were no drug-related serious adverse events reported. Symptoms and sensitivities typically associated with triptans were rare and similar to placebo. Additional analyses indicated the potential of LEVADEX to effectively treat any time during the migraine including four to eight hours after onset of migraine. In 2010, we announced that a second Phase 3 clinical trial would not be required for the LEVADEX NDA submission, completed and announced successful results from a PK trial in smokers, a PD trial evaluating pulmonary artery pressure using echocardiogram and a thorough QT trial. In addition, we completed our 12 month open-label safety extension of the Phase 3 FREEDOM 301 trial. In this trial no drug related serious adverse events were reported. The LEVADEX clinical development program evaluated the efficacy, safety, PK

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and PD of LEVADEX in approximately 1,000 patients. We plan to submit an NDA to the FDA in the first half of 2011. Based on these results, we believe LEVADEX has the potential to be suitable as a first-line therapy for some migraine patients.

Migraine

Background

Migraine is a chronic and debilitating neurological disorder characterized by episodic attacks. Migraine attacks typically manifest themselves as moderate to severe headache pain, with associated symptoms that often include nausea and vomiting, photophobia, phonophobia, and visual disturbances or aura. They usually involve pounding or throbbing pain on one side of the head, although pain may occur on both sides. Migraines limit the normal functioning of patients, who often seek dark, quiet surroundings until the episode has passed. Most migraines last between four and 24 hours, but some last as long as three days. According to published studies, the median frequency of attack is 1.5 times per month, although approximately 25% of migraine sufferers experience one or more attacks every week.

Prevalence

Migraine is a major public health problem that affects up to approximately 12% of the population in the United States and approximately 15% in Europe. According to the National Headache Foundation, approximately 30 million people in the United States suffer from migraine. Migraine is more common in women, with about 18% of women affected and 6% of men. Migraine prevalence is highest during the peak productive ages of 25 to 55, which results in high costs to employers and managed care organizations.

Migraine disability and economic impact

Migraine is listed in the top 20 causes of disabling conditions and in the top four neurologic disabling conditions by the World Health Organization (WHO). Related disability from migraine is substantial, with over 90% of sufferers experiencing functional impairment with their migraine that can disrupt every aspect of day to day life, including work, school, family and social relationships. More than half of sufferers report severe impairment or the need for bed rest as a result of their migraines, according to published surveys. The economic burden of migraine remains substantial despite existing treatments with migraine patients losing four to six work days each year due to headache. The combination of direct and indirect costs of migraine in the United States is estimated at over $20 billion annually.

Current treatments

There are two general categories of migraine therapies: acute and preventive. Acute therapies dominate the migraine market and are used during infrequent attacks, typically characterized as one to three attacks per month, and are designed to relieve the pain, nausea, phonophobia and photophobia symptoms of migraine. The goals of acute therapy are to stop the attack quickly and consistently, while preventing recurrence, to maintain the patient s ability to function, to use the least amount of medication and to limit adverse side effects. Although triptans are the predominant class of drugs used to specifically target migraine, DHE is another class of acute, migraine-specific therapy.

Migraine preventative and prophylactic therapies are designed to reduce the frequency and severity of migraine attacks, to make acute migraine attacks more responsive to acute therapies and to improve the quality of life for patients. Topiramate is the market leader among preventive drugs. Other drug categories used in migraine prophylaxis include beta blockers, tricyclic antidepressants and calcium channel blockers.

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Prescribers of migraine therapies

Most migraine patients are first diagnosed, treated and managed by primary care physicians and internists. Referral to a neurologist or headache specialist usually occurs when the patient suffers more frequent, severe and disabling migraines. There are approximately 10,000 neurologists in the United States and they are responsible for nearly 20% of the triptan prescriptions written. About half of the neurologists account for over 90% of the triptan prescriptions written by this specialty, making a specialized sales force strategy executable.

Market size

In 2008, according to market data, approximately 29 million prescriptions were written for the treatment of migraine in the United States. Approximately 12 million of those prescriptions were written for acute migraine specific drugs. The majority of acute migraine specific drug prescriptions written were in the triptan class. In 2010, the triptan market in the United States totaled approximately $1.6 billion in revenues. The triptan with the largest market share is sumatriptan with 2010 prescriptions of approximately 6.1 million in the United States.

Limitations of Current Migraine Therapies

The type of migraine treatment prescribed depends on the frequency and severity of the headache, speed of onset and previous response to medication. In published studies, migraine sufferers often cite faster onset of pain relief and lower incidence of migraine recurrence as two key therapeutic attributes they would like from their medication. Treatment typically involves patients self-medicating with over-the-counter drugs when pain is mild and attacks are infrequent. Patients with more frequent or severe migraine or those who do not respond to simple analgesics may seek medical attention with a primary care physician initially and then with a headache clinic or neurology specialist, if needed. Once a physician has diagnosed migraine, triptans are generally prescribed. If a patient does not respond to one triptan, the physician may switch to another, as the response to various triptans is unpredictable.

Triptans have three major limitations:

Slow and variable onset of action and short duration of effect: While triptans have improved the treatment of migraine, the onset of pain relief with these products tends to be relatively slow and variable due to inconsistent systemic absorption via oral and nasal routes of administration. Published studies cite that recurrence of migraine, or the recurrence within 24 hours of an effectively treated migraine, is a common reason given for dissatisfaction among migraine sufferers.

Not broadly efficacious: Approximately 30% to 40% of migraine patients do not fully respond to the first triptan prescribed. Migraine patients who do not respond to any triptan therapy have few satisfactory alternatives. Additionally, triptans have been shown to be more effective when taken early in a migraine attack; however, migraine sufferers often wait to treat or are unable to treat early and may not fully benefit from triptan therapy.

Side effects: Triptans may produce sensations of chest tightness, chest pressure and tingling, often referred to as triptan sensations.

DHE is an acute therapy and alternative to triptans that has been used for more than 50 years to safely treat migraine. Many headache specialists consider DHE to be the standard of care in treatment of status migrainosus, which is a condition characterized by debilitating migraines that last more than 72 hours. Although DHE overcomes many of the limitations of triptans, historically it also has had its own limitations, including the following:

Inconvenient and inconsistent dosing: DHE has been available predominantly for administration intravenously and nasally. Intravenous administration of DHE requires the supervision of a healthcare provider and is typically performed in a headache clinic or hospital setting, which is expensive and requires the patient to travel to one of these locations while suffering with the migraine. Absorption of DHE via the nasal pathway may lead to inconsistent dosing, and generally takes 30 to 60 minutes to

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provide significant pain relief. Nasal administration of DHE may result in unpleasant taste, and can cause congestion or irritation of the nasal membrane.

Side effects: One of the common side effects of DHE administered intravenously is nausea. Patients who receive DHE intravenously are often given an anti-nausea medication at the same time.

Our Potential Solution: LEVADEX

Based on our Phase 3 FREEDOM-301 clinical trial, we believe that LEVADEX may provide patients with the following benefits when compared to existing migraine therapies:

Rapid onset: In our Phase 3 clinical trial, LEVADEX provided significant pain relief at 30 minutes after dosing and pain relief in as early as 10 minutes for patients with severe migraine pain.

Long-lasting: In our Phase 3 clinical trial, LEVADEX provided long-lasting pain relief with low incidence of recurrence, and provided sustained pain relief through 48 hours.

Efficacy at any time after the start of migraine: Additional analyses indicated the potential of LEVADEX to effectively treat at any time during the migraine including within one hour, and after eight hours from the start of migraine.

Broadly efficacious: Based on historical DHE use, LEVADEX may provide a higher response rate and has the potential to treat patients who have not previously responded to other therapies, such as triptans. We also believe that LEVADEX has the potential to treat a broad spectrum of migraine, including migraine subpopulations that are often difficult to treat, such as menstrual migraine, morning migraine, migraine with allodynia, migraine associated with severe pain and migraine with nausea and vomiting.

Low incidence of side effects: In our Phase 3 clinical trial, LEVADEX was well tolerated, with the most common adverse event reported being medication aftertaste at 6% compared with 2% for placebo. The next most common adverse event was nausea at 5%, compared with 2% for placebo. Symptoms or sensitivities typically associated with commonly used triptan migraine treatments, such as chest discomfort or chest pain, were rare and comparable to placebo.

Convenient and consistent delivery: LEVADEX is non-injectable and designed to be easy to use, which may result in increased patient comfort and compliance. The clinical trial was performed in the home, without clinical supervision and with minimal training. In a previous trial, dose-to-dose variability was comparable to solid oral dosage forms.

LEVADEX Clinical Development Program

We completed our LEVADEX clinical development program in 2010. Our program evaluated the efficacy, safety, PK and PD of LEVADEX in approximately 1,000 patients. In 2010, we announced that a second Phase 3 clinical trial would not be required for our NDA submission, completed and announced successful results from a PK trial in smokers, a PD trial evaluating pulmonary artery pressure via echocardiogram and a thorough QT trial. In addition, we completed our 12 month open-label safety extension of the Phase 3 FREEDOM 301 trial.

Phase 3 Clinical Program. We evaluated the safety and efficacy of LEVADEX as a potential acute treatment for migraine in a Phase 3 multi-center, randomized, double-blind, placebo-controlled or FREEDOM 301 trial followed by a 12-month open-label safety assessment. In this trial, patients were randomized to either LEVADEX or placebo during the efficacy portion of the trial.

In May 2009, we announced results of the efficacy portion of FREEDOM-301. 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.

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Patients taking LEVADEX therapy had statistically significant improvement at two hours compared to patients on placebo for each of the primary endpoints:

- Pain relief: 58.7% of patients who received LEVADEX compared with 34.5% for placebo ($p<0.0001$);
- Phonophobia free: 52.9% of patients who received LEVADEX compared with 33.8% for placebo ($p<0.0001$);
- Photophobia free: 46.6% of patients who received LEVADEX compared with 27.2% for placebo ($p<0.0001$); and
- Nausea free: 67.1% of patients who received LEVADEX compared with 58.7% for placebo ($p=0.02$).

A total of 792 patients were included in the primary data analysis as specified in the protocol of the FREEDOM-301 study. The patient population studied had more severe migraine pain than expected, with 46% reporting severe pain and 54% reporting moderate pain prior to administration of the study drug.

Results from additional pre-defined analyses include:

- LEVADEX therapy achieved statistically significant onset of pain relief at 30 minutes after dosing ($p=0.03$);
- While not statistically significant, 50% more of the patients receiving LEVADEX therapy than the patients receiving placebo reported pain relief at 10 minutes;
- LEVADEX therapy achieved statistically significant sustained pain relief from two to 24 hours ($p<0.0001$), as well as two to 48 hours ($p<0.0001$, when unadjusted for multiplicity);
- LEVADEX therapy achieved statistically significant pain freedom (pain symptom score = 0) as early as 30 minutes ($p=0.002$, when unadjusted for multiplicity); and
- LEVADEX therapy achieved sustained pain freedom from two to 24 hours, as well as two to 48 hours ($p<0.0001$ for both time points, when unadjusted for multiplicity).

LEVADEX was well tolerated, with the most common adverse event reported being medication aftertaste at 6%, with 2% of patients receiving placebo also reporting medication aftertaste. The next most common adverse event was nausea at 5%, compared with 2% for placebo. Symptoms or sensitivities typically associated with commonly used triptan migraine treatments, such as chest discomfort (1%) or chest pain (0%), were rare and comparable to placebo. There were no decreases in lung function, as measured by spirometry, between the active and placebo groups. There were no drug-related serious adverse events reported in the trial. These data were presented in September 2009 in a late-breaking session of the 14th Congress of the International Headache Society.

In September 2009, we announced that post-hoc analysis of data from this Phase 3 trial shows the potential of LEVADEX to be effective in treating acute migraine as well as a broad spectrum of migraine, including migraine subpopulations that are often resistant to current therapies such as triptans, migraine with moderate and severe pain, migraine with nausea and vomiting and migraine with and without aura.

In October 2009, we announced that we had completed a planned interim safety review of the open-label, long-term safety extension of FREEDOM 301. At that point, more than 400 patients had completed at least six months of treatment and over 7,800 headaches had been treated in the safety extension. No drug-related serious adverse events had been reported. The goal of the ongoing long-term safety extension was to evaluate overall safety, including pulmonary and cardiovascular safety, of LEVADEX in at least 300 patients for six months and in at least 150 patients, including migraine sufferers with asthma, for 12 months as part of a potential NDA. The interim review of the data was conducted after a pre-specified number of patients had completed six months of exposure to LEVADEX and was also reviewed by an independent Data Monitoring Committee, or DMC. The

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DMC is an independent group of clinical trial experts, including physicians, formed to critically review and evaluate patient safety data generated in the FREEDOM 301 trial with the objective of ensuring clinical trial patient safety, quality of the data collected and continued scientific validity of the trial design. On an ongoing basis, the DMC reviewed data from the safety extension, including results of both pulmonary lung function evaluations using measures such as DLco and FEV_1 and cardiac evaluations using electrocardiograms, echocardiograms and chest X-rays.

In January 2010, we announced that the FDA had informed us that a second pivotal efficacy study would not be required for the LEVADEX NDA submission.

In July 2010, we announced results from a clinical trial comparing the PK and safety of LEVADEX and intravenous DHE in 23 smokers and 24 non-smokers. The trial was designed to measure whether systemic absorption and exposure in smokers is greater 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.

In September 2010, we announced results from a PD trial evaluating pulmonary artery pressure in approximately 24 healthy volunteers using echocardiogram. The trial compared 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 September 2010, we also announced in connection with our ongoing open-label safety trial: more than 400 patients had completed at least six months of treatment and more than 200 patients had completed twelve months of treatment; all non-asthmatic patients and a subset of asthmatic patients had completed treatment; LEVADEX was well tolerated and no drug-related serious adverse events had been reported; and no clinically significant trends had been reported for LEVADEX in the evaluation of cardiovascular measurements and pulmonary function.

In November 2010, we announced results from a thorough QT trial in 54 healthy adults comparing the acute effects of a supra-therapeutic dose of LEVADEX (approximately three times the anticipated commercial dose), oral moxifloxacin (400 mg) and placebo on the cardiac QT interval as measured by electrocardiogram. Results of the trial showed that a supra-therapeutic dose of LEVADEX does not increase QTc intervals. For the supra-therapeutic dose of LEVADEX, the largest mean difference from placebo in QTc (using the individual correction method for heart rate, or QTci) was 0.08 milliseconds, and the largest one-sided 95% upper confidence bound was 2.24 milliseconds. The threshold level of regulatory concern is when the change produced by a drug has a 95% upper confidence bound that exceeds 10 milliseconds. The number of subjects with individual QTc intervals > 450 milliseconds and increases in QTc from baseline > 30 milliseconds were similar to placebo. Moxifloxacin, the positive control, produced QT prolongation consistent with previous thorough QT trials.

In December 2010, we announced completion of the LEVADEX open-label safety trial. In total, more than 475 patients completed six months treatment and more than 250 patients completed 12 months treatment. No drug-related serious adverse events were reported. We have now completed the final trial necessary to support an NDA for LEVADEX and plan to submit the NDA in the first half of 2011.

Phase 2 Clinical Trial Results. In March 2007, we announced positive results from two Phase 2 clinical trials with LEVADEX for the acute treatment for migraine.

The objective of the first Phase 2 clinical trial was to evaluate the efficacy and tolerability of three different doses of LEVADEX in adult migraine patients when self-administered at home. This Phase 2 clinical trial was a randomized, double blind, placebo-controlled trial of three doses of LEVADEX in 86 patients. The clinical trial consisted of two treatment periods. The first treatment period evaluated two doses of LEVADEX, 1.0 mg and 0.5 mg versus placebo and the second treatment period re-randomized responders in the first treatment period to

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evaluate a lower dose, 0.25 mg versus placebo. In the first treatment period, the 0.5 mg dose of LEVADEX showed pain relief in 32% of the patients at ten minutes (p = 0.019), pain relief in 72% of the patients at two hours, the clinical trial s primary endpoint (p = 0.019), and sustained pain relief in 43% of the patients at 24 hours (p = 0.066) in a treatment received population. Unlike IV DHE, which is generally administered with an anti-nausea medication, LEVADEX was administered by itself and showed no statistically significant drug related increase in nausea. LEVADEX was also shown in the clinical trial to be well tolerated, with no serious adverse events reported. In the second treatment period, 35 subjects were randomized to treat a second subsequent migraine with a 0.25 mg dose versus placebo. No significant benefit was seen with this lowest dose when compared to placebo.

The objective of the second Phase 2 clinical trial was to evaluate the safety and tolerability of LEVADEX in subjects with asthma and to demonstrate that the blood levels of the drug achieved by the therapy were similar to those seen after inhalation by subjects with healthy lungs. This Phase 2 clinical trial was a randomized, double blind, placebo-controlled trial in 19 adult asthmatics. Each patient received three doses, one every week in randomized order over a 15-day period, including two 1.0 mg doses of LEVADEX and one dose of placebo. The clinical trial indicated that LEVADEX was well tolerated by subjects with compromised lung function, and that the PK of LEVADEX, or distribution of the drug in the body, was similar to that experienced by adults with healthy lungs as shown in an earlier Phase 1 clinical trial. No serious or significant drug related adverse events were reported. In addition, no clinically significant changes were observed in pulmonary function tests, heart rate, blood pressure, respiratory rate or mean IgE levels, a measure of systemic immune response, or the body s defenses reacting to a foreign substance.

We believe that, based on our PK and receptor binding research, administration of LEVADEX via the lung may provide an opportunity to retain the efficacy attributes seen with IV DHE while minimizing the potential side effects often seen during IV DHE administration. PK data suggest that LEVADEX closely mimics the blood levels and the time to maximum drug concentration seen with effective doses of DHE administered intravenously. However, unlike IV administration of DHE, we do not expect LEVADEX to cause significant treatment related nausea which may be a factor that has limited the usage of IV DHE outside the headache clinic or hospital. In the FREEDOM 301 trial the incidence of treatment related nausea was low at 5% compared with 2% for placebo. In our Phase 1 trial comparing IV DHE to LEVADEX, the blood levels of drug were similar. However, the maximum drug concentration for inhaled DHE administered with our TEMPO inhaler was approximately 40 fold lower than that for IV DHE, which we believe in part accounts for the low incidence of drug-induced nausea observed in our clinical trials to date.

In addition, we have conducted pre-clinical animal studies to evaluate lung toxicity and coronary vascular effects of our proprietary formulation of DHE. In our six month chronic inhalation toxicity assessment of DHE, where animals were exposed to up to 1.08 mg/kg (more than 46 times the maximum potential recommended daily dose of LEVADEX, if approved) of DHE per day for six months, there was no significant respiratory tract toxicity observed. In another pre-clinical study designed to evaluate cardiovascular parameters, we observed no significant differences in coronary vascular effects comparing inhaled DHE to IV DHE.

Because DHE is well characterized and previously approved, we may seek FDA marketing approval of LEVADEX under Section 505(b)(2) of the FFDCA. Section 505(b)(2) of the FFDCA provides an alternate path to FDA approval for modifications to formulations of products previously approved by the FDA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from clinical trials not conducted by or for the applicant and for which the applicant has not obtained a right of reference. This may expedite the development program for LEVADEX by potentially decreasing the overall scope of work we must do ourselves.

Other Potential Uses and Indications for LEVADEX

We plan to consider development of LEVADEX for use outside the United States as well as for potential additional indications beyond acute migraine.

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We believe there is opportunity to develop LEVADEX for potential use outside of the United States. While acute migraine is a major public health problem affecting approximately 12% of the population in the United States, it also affects approximately 15% of the population in Europe. Based on the accumulated nonclinical and clinical data to date, we believe there may be significant commercial opportunities for LEVADEX outside of the United States.

Furthermore, based on key LEVADEX attributes observed to date, including fast onset of action, long duration of effect as well as historical uses for DHE, developing additional indications for LEVADEX may represent significant opportunities. We believe LEVADEX may have the potential to treat additional migraine indications such as cluster headache, menstrual migraine, adolescent migraine, chronic migraine, chronic daily headache, medication over-use headache and status migrainosus.

Other Product Technologies

While we do not plan to make further significant direct investment in the product candidates described below, we plan to evaluate other potential product candidates which may utilize these technologies, as well as partnership opportunities for further development and commercialization of these product candidates.

Nebulized Corticosteroid Particle Technology

We have expertise in the formulation of nebulized corticosteroids for the treatment of pediatric asthma. We have created novel versions of budesonide that are designed to be administered more quickly and to provide efficacy at lower doses than conventional nebulized budesonide. Conventional nebulized budesonide is an inhaled corticosteroid approved by the FDA, for treating asthma in children from 12 months up to eight years of age. We have developed novel morphologies of corticosteroid particles which may allow for faster delivery and efficacy at a lower dose, which together may offer improved safety, compliance and convenience.

We have suspended development of Unit Dose Budesonide, our former nebulized budesonide program, after not meeting primary efficacy endpoints in a Phase 3 trial. However, we believe our technology remains applicable. We are considering options moving forward, by leveraging our experience with budesonide and our expertise in particle technology, including the development of a next generation therapy with a corticosteroid.

MAP0005 Combination Particle Technology

We believe MAP0005 serves as a proof of concept for the robust, specific delivery of two therapeutic agents that could benefit from targeted receptor delivery in a fixed ratio within a single particle. We intend to opportunistically evaluate the application of this technology to additional product candidates because we believe our proprietary technologies in this area have potential broad applicability for a number of combination product candidates in diverse indications via inhalation and other routes of delivery. MAP0005, our proprietary combination of an inhaled corticosteroid and a long-acting beta-agonist, or LABA, for the potential treatment of asthma and chronic obstructive pulmonary disease, or COPD, utilizes our proprietary particle formulation technologies to administer the optimal ratio of multiple drugs in a reproducible and consistent manner. We combine two or more drugs together into a single micron scale inhalable particle at a pre-defined consistent and reproducible ratio, which may improve the delivery profile and stability of the resultant combination therapy. In April 2008, we announced positive results from a Phase 2a clinical trial evaluating MAP0005 for the potential treatment of asthma and COPD. We believe this approach, as compared to current ICS/LABA combinations, may allow the optimal ratio of each drug to the lung to reach the relevant receptors at the cellular level in the lung in a more reproducible and consistent manner, reducing the amount of drug delivered systemically and potentially improving the side effect profile, while improving therapeutic efficacy.

MAP0001 Stable Protein and Peptide Particle Technology

We believe MAP0001 serves as proof of concept for the ability to formulate and stabilize biologically-active proteins and peptides and deliver them to the lung. We design and incorporate our protein formulations

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without the need for excipients or other additives, to be stored for months at room temperature and to provide multiple doses of medicine delivered accurately without the need for invasive needle injections. We intend to opportunistically evaluate the application of this technology to additional product candidates. We are demonstrating this capability with MAP0001, our proprietary formulation of insulin for the potential treatment of Type 1 and Type 2 diabetes via pulmonary delivery using our proprietary TEMPO inhaler. In a Phase 1a clinical trial conducted in Australia, MAP0001 was biologically active and achieved maximum therapeutic blood levels as quickly as Novorapid subcutaneous injection, a widely used injectable insulin.

We have not filed an IND with the FDA for MAP0005 or MAP0001 because our clinical trials were not conducted in the United States.

Our Technology

Our aerosol delivery and pharmacological profiling technology combines our knowledge of aerosol science and medicine, and enables us to create inhaled drug products with potentially enhanced pharmacological profiles relative to the parent drugs, thereby improving their efficacy and safety. Starting with the bulk drug substance, we develop particles with physical and chemical characteristics that are well suited for the aerosol delivery of the product candidate. The particle engineering allows more of our drug to reach the areas of the respiratory tract to treat disease and reduces the amount of drug that is deposited in the back of the throat where it can cause local and systemic side effects. We then formulate the drug particles into a delivery medium and package them into the aerosol delivery system that is best suited for the formulation and dosing regimen in order to maximize patient compliance. Our expertise in aerosol formulation science and pulmonary medicine allows us to select excipients, if any, already in wide use and regarded as safe, that result in favorable safety characteristics and allow flexibility in delivery format. The resulting drug products can be as consistent and efficient as alternative, often more invasive dosing formats, such as injection, but with the advantages of fast onset, high degree of intake at the target organs, and lower or controlled systemic exposure. The convenience, consistency and efficiency of inhaled administration in combination with the characteristics of our product candidates can offer meaningful therapeutic benefits when compared to existing drugs, increasing the probability of the successful adoption of our product candidates.

We apply our proprietary technologies to optimize drugs for two general types of therapeutic applications:

Pulmonary delivery as a non-invasive method of quickly and safely administering systemic drugs. Administration of drugs via the respiratory tract is a non-invasive method of delivering drugs efficiently to the systemic circulation, with rapid onset of action, bypassing the gastrointestinal tract where many drugs are extensively metabolized after oral administration, and with rapid onset of action. The drug, or combination of drugs, can reach the intended site of action as quickly as intravenously administered drugs and more quickly than oral, dermal, sublingual or even alternative injection routes, such as subcutaneous or intramuscular. We can apply our technology to small or large molecules, including peptides and proteins.

Delivery of drugs to treat respiratory diseases locally. Diseases such as asthma, COPD and some respiratory tract infections have been treated by pulmonary drug delivery for many years in order to target therapeutic effect to the lung and reduce systemic drug exposure and related side effects. Our technology is designed to improve the therapeutic efficacy and safety of known drugs for these applications, by efficiently delivering customized drug particles to those areas in the lung where drug is required and minimizing the drug exposure to other areas of the respiratory tract and body. In addition, our technologies have the potential to broaden the types of respiratory illnesses that can effectively be targeted and treated safely via pulmonary delivery.

Aerosol Delivery and Pharmacological Profiling Technology

Our proprietary technologies include particle creation and formulation technologies, which can be applied to small or large molecules, including peptides and proteins. Our technologies also include the development and

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manufacturing of aerosol delivery platforms, including our TEMPO inhaler. The TEMPO inhaler is a proprietary, next generation pressurized metered dose inhaler, or MDI, that dispenses drug automatically when the patient inhales and has high consistency and efficiency compared to other inhalers. Our technologies are covered by over 15 issued U.S. patents and over 25 U.S. patent applications that we own or have licensed, as well as their foreign counterparts.

Particle Creation and Formulation

We control the characteristics of our drug particles by using technology and expertise in aerosol physics, particle science and formulation, and in safety toxicology and pharmacology. We can consistently generate drug-containing aerosols with the optimal particle or droplet sizes for the therapeutic indication. Particles that are too large tend to be deposited in the throat, while medium sized particles are more efficiently delivered to the large bronchial tubes and small particles are more efficiently delivered to the alveoli, the small sacks that make up most of the absorptive surface area of the lung. We can formulate product candidates in propellants without additional excipients, or with small amounts of excipients previously shown to be safe. We can also combine drugs by producing small, inhalable particles composed of one drug which is reproducibly intermingled or coated with multiple drugs in fixed ratios.

One of our key technologies is the generation of particles by supercritical fluid, or SCF, crystallization. SCF gives us the ability to create very small particles ranging from 100 nanometers to 10 microns in diameter with highly precise particle size distributions. The particles have uniform surfaces with few discontinuities or irregularities that provide enhanced aerosol performance. They are also stable for long storage periods without refrigeration, and require minimal or no excipients that can increase the potential for local toxicity or inflammatory response.

In addition to particle generation, we have extensive expertise in formulating aerosol drugs, especially for nebulized and MDI delivery formats. A key feature of this expertise is our know-how in formulating aerosolized drugs with appropriate excipients. We have expertise in formulation screening, assay development, aerosol performance testing and clinical performance simulation, long-term stability testing, large volume non-clinical testing and generation and release of pre-clinical and clinical supplies through to human clinical proof of concept.

We believe that the combination of these various particle creation and formulation technologies is a key component of our competitive advantage.

TEMPO Inhaler Platform

We designed our proprietary TEMPO inhaler to enable accurate and reproducible pulmonary delivery of the drug particles we develop. Our TEMPO inhaler is an innovative next generation MDI. The TEMPO inhaler incorporates the size, ease of use and convenience advantages associated with standard MDIs, and is designed to overcome their greatest limitations: inconsistent dosing, drug delivery inefficiency and the need for patients to synchronize a breath with manual triggering of the inhaler, which is particularly difficult for certain patient populations. Even the more recently introduced breath-actuated MDIs exhibit the inconsistent dosing and drug delivery inefficiency of older MDIs.

The TEMPO inhaler is designed to offer a number of key competitive advantages compared to standard MDIs. These advantages include:

Automatic, optimal release of therapy: Our triggering technology is tuned for each particular drug so that drug release is synchronized to the optimal point in the breathing cycle to allow the released drug to reach the targeted area of the respiratory tract. For example, data from a scintigraphy study showed that the TEMPO inhaler deposited 75% less of a corticosteroid in the mouth and throat and delivered three times as much drug to the lungs as a conventional MDI.

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Plume speed control: Conventional MDIs spray plumes of drug at speeds of up to 50 miles per hour, causing much of the drug to hit the back of the throat. By contrast, our TEMPO inhaler controls and slows down the drug plume to match the speed of the patient s inhaled breath, so more of the drug is entrained in the inhaled air and carried into the lungs.

Dose consistency: Results from the TEMPO inhaler performance data along with results from our clinical trials indicate that the TEMPO inhaler s dose-to-dose consistency is comparable to IV dosing. The TEMPO inhaler also includes a dose counter to display how many doses remain available for use. The dose counter can prevent dispensing of additional doses after a maximum number of doses have been delivered.

Convenient, multiple dose use: The TEMPO inhaler does not use electronics or batteries and can conveniently contain multiple doses. It can include up to a month s supply depending on the drug, in a small, handheld inhaler approximately the same size as a conventional MDI and it may be used with small molecule drugs and biologics.

We have conducted clinical trials with three clinical product candidates which utilize our TEMPO inhaler: LEVADEX for the potential treatment of mig