NUPATHE INC.
Form 10-K
March 18, 2011

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

FORM 10-K

(Mark One)

þ **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

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission file number 001-34836

NuPathe Inc.
(Exact name of registrant as specified in its charter)

Delaware	**20-2218246**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification number)
227 Washington Street Suite 200 Conshohocken, Pennsylvania	**19428**
(Address of principal executive offices)	(Zip Code)

Registrant s telephone number, including area code: (484) 567-0130

Securities registered pursuant to Section 12(b) of the Securities Exchange Act of 1934:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.001 par value per share	**The NASDAQ Stock Market LLC (The NASDAQ Global Market)**

Securities registered pursuant to Section 12(g) of the Securities Exchange Act of 1934:
None

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

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

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

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

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

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

Large accelerated filer o	Accelerated filer o	Non-accelerated filer þ	Smaller reporting company o

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the last sale price or the average bid and asked price of such common equity, as June 30, 2010 is not provided because the registrant s common equity did not commence trading on The NASDAQ Global Market until August 6, 2010.

As of February 14, 2011, 14,549,461 shares of the registrant s common stock, $0.001 par value per share, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive Proxy Statement for its 2011 Annual Meeting of Stockholders are incorporated by reference into Part III of this Form 10-K to the extent stated herein. Such Proxy Statement will be filed with the Securities and Exchange Commission within 120 days after the end of the fiscal year to which this Form 10-K relates.

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Annual Report on Form 10-K for the Fiscal Year Ended December 31, 2010
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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this Form 10-K that are not historical facts are hereby identified as forward-looking statements for this purpose and include, among others, statements relating to:

- our plans to develop and commercialize Zelrix and our other product candidates;
- the timing of, and our ability to obtain, marketing approval of Zelrix and our other product candidates;
- the timing of our anticipated commercial launch of Zelrix and our other product candidates;
- our ongoing and planned preclinical studies and clinical trials;
- the rate and degree of market acceptance of Zelrix and any other future products;
- the size and growth of the potential markets for Zelrix and our other product candidates and our ability to serve those markets;
- our commercialization and marketing capabilities;
- our ability to obtain and maintain intellectual property protection and the scope of such protection;
- legal and regulatory developments in the U.S. and foreign countries;
- the performance of third party manufacturers;
- our ability to establish and effectively manage a supply chain;
- our ability to acquire or license suitable product candidates or technologies from third parties;
- future expenses and capital requirements;
- the sufficiency of our cash and cash equivalents to fund our operations and capital requirements through FDA approval and into the expected commercial launch of Zelrix in the first half of 2012; and
- our ability to raise additional capital in sufficient amounts or on terms acceptable to us;

as well as other statements relating to our projections, expectations, beliefs, future performance or plans or objectives for future operations (including assumptions underlying or relating to any of the foregoing). Forward-looking statements may appear throughout this Form 10-K, including without limitation, in the following sections: Item 1 Business, Item 1A Risk Factors, Item 7 Management s Discussion and Analysis of Financial Condition and Results o Operations, and Item 8 Financial Statements and Supplementary Data. Forward-looking statements generally can be identified by words such as may, will, could, would, should, expect, intend, plan, anticipate, believ project, potential, continue, ongoing and similar expressions, although not all forward-looking statements con these identifying words.

Forward-looking statements are based upon our current expectations and beliefs and are subject to risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this Form 10-K, and in particular the risks and uncertainties discussed under the caption Risk Factors and those discussed in other documents we file with the Securities and Exchange Commission (SEC). As a result, you should not place undue reliance on forward-looking statements.

Additionally, the forward-looking statements contained in this Form 10-K represent management s views as of the date of this Form 10-K (or any earlier date indicated in such statement). While we may update certain forward-looking statements from time to time, we specifically disclaim any obligation to do so, whether as a result of new information, future developments or otherwise. You are advised, however, to consult any further disclosures we make on related subjects in our periodic and current reports to the SEC. The foregoing cautionary statements are intended to qualify all forward-looking statements wherever they may appear in this Form 10-K.

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PART I

ITEM 1. BUSINESS

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of branded therapeutics for diseases of the central nervous system, including neurological and psychiatric disorders. We were incorporated in the State of Delaware in January 2005. Our most advanced product candidate, Zelrix, is a single-use, transdermal system applied as a patch to the upper arm or thigh for the treatment of acute migraine. Zelrix incorporates our proprietary SmartRelief technology. SmartRelief uses a mild electrical current to actively deliver sumatriptan through the skin in a process called iontophoresis.

We submitted a New Drug Application, or NDA, for Zelrix to the United States Food and Drug Administration, or FDA, in October 2010. The NDA is supported by Phase III clinical data in which Zelrix was evaluated in 796 patients and 8,913 migraines. The Prescription Drug User Fee Act date, or PDUFA date, for our NDA is August 29, 2011. The PDUFA date is the target date for the FDA to complete its review of the NDA. If approved, Zelrix will be the first transdermal patch for the treatment of migraine. Subject to the approval of our NDA, we plan to build our own specialty sales force in the U.S. to launch Zelrix.

Migraine is a debilitating neurological disease that affects approximately 31 million people in the U.S. In 2010, according to IMS Health Inc., or IMS, a leading provider of pharmaceutical industry market data, U.S. sales of prescription products for migraine exceeded $1.7 billion, over 97% of which were for a class of medication called triptans. Sumatriptan, the active ingredient in Zelrix, is the most prescribed triptan and is currently available in oral, nasal and injectable formulations

In a majority of their migraines, most patients suffer from one or more significant gastrointestinal problems, which include nausea, vomiting and a compromised ability to digest, known as decreased gastric motility. Nausea and vomiting impede the use of oral medications, while reduced gastric motility can result in low and inconsistent absorption of oral medications which we believe may cause migraine patients, or migraineurs, to fail to respond consistently to such medications.

The American Academy of Neurology, or AAN, guidelines recommend a non-oral route of administration for migraineurs who experience nausea or vomiting as significant migraine symptoms. Despite this recommendation and the prevalence of nausea and vomiting, IMS reported that non-oral formulations comprised only 4% of triptan units sold in the U.S. in 2010. We believe the frequency of adverse events associated with non-oral migraine treatments, such as nasal and injectable formulations, contributes to the low adoption rate of these medications.

We believe Zelrix will be an attractive treatment option for migraineurs who suffer from nausea or vomiting with migraine and for those who experience inconsistent relief or adverse events from their current treatment because Zelrix was designed to:

- *Circumvent nausea and vomiting.* Because Zelrix is administered transdermally, we believe that nausea and vomiting relating to a migraine will not impede its use.
- *Increase consistency of response.* Because Zelrix does not depend on gastrointestinal absorption, its absorption will not be compromised by the reduced gastric motility experienced by some migraineurs. As a result, we believe that Zelrix will provide more consistent relief than oral medications.
- *Minimize triptan adverse events.* Because Zelrix tightly controls the delivery of sumatriptan, we believe its use will result in a low incidence of triptan adverse events while effectively treating migraine as demonstrated in our clinical trials.

We also have two other proprietary product candidates in preclinical development that address large market opportunities, NP201 for the continuous symptomatic treatment of Parkinson s disease and NP202 for the long-term treatment of schizophrenia and bipolar disorder.

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Our Product Candidates

The following table summarizes key information about our existing product candidates. We hold worldwide commercialization rights to all of our product candidates.

Product Candidate	Indication(s)	Description	Development Status
Zelrix	Acute migraine	Active, single-use sumatriptan transdermal patch	NDA submitted in October 2010. PDUFA date is August 29, 2011. One ongoing long-term, open label Phase III trial.
NP201	Parkinson s disease	Ropinirole two-month implant	Expected Investigational New Drug submission during first half of 2011. Preclinical proof of concept completed.
NP202	Schizophrenia and bipolar disorder	Atypical antipsychotic three-month implant	Expected Investigational New Drug submission in 2012. Prototype development in progress.

Migraine Market

Overview

Migraine is a debilitating neurological disease that affects approximately 31 million people in the U.S. Symptoms of migraine include moderate to severe headache pain, nausea and vomiting, photophobia, or abnormal sensitivity to light, and phonophobia, or abnormal sensitivity to sound. Most migraines last between four and 24 hours, but some last as long as three days. According to an article by Dr. Richard Lipton published in 2007 in *Neurology*, a peer-reviewed medical journal, 63% of migraineurs experience between one and four migraines per month, and 31% of migraineurs experience three or more migraines per month. Migraineurs are limited in their daily function during a migraine and often seek dark, quiet surroundings until the migraine has passed.

According to another article by Dr. Richard Lipton, published in 2001 in *Headache*, a peer-reviewed medical journal, over 18% of women and over 6% of men in the U.S. experience migraines. Lipton further reported that migraines are most common in the working population, from 25 to 55 years old, and can be sufficiently serious to cause migraineurs to miss work or school. According to an article by Dr. Kevin Hawkins published in 2008 in *Headache*, estimated direct medical expenditures for migraine, including outpatient costs, pharmaceutical costs, inpatient costs and emergency department costs, exceed $11.0 billion per year in the U.S.

Over 13 million prescriptions for medications indicated for acute migraine were filled in the U.S. in 2010, according to IMS. More than 90% of these prescriptions were for triptans. Triptan sales in the U.S. in 2010 equaled $1.7 billion, with approximately 123 million individual units sold.

Migraine-Associated Nausea and Vomiting

Symptoms other than headache pain contribute significantly to the disability caused by acute migraine. In particular, nausea and vomiting during a migraine can be severe and incapacitating. According to an article by Dr. Stephen Silberstein published in 1995 in *Headache*, 92% of migraineurs have experienced nausea at least once during a migraine, and 56% of these migraineurs experience nausea in a majority of migraines. Silberstein also reported that 68% of migraineurs have experienced vomiting at least once during a migraine, and 32% of these migraineurs experience vomiting in a majority of migraines. Accordingly, these data indicate that 52% of all migraineurs experience nausea in a majority of migraines and 22% of all migraineurs experience vomiting in a majority of migraines.

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Migraine-Associated Gastroparesis

According to an article by Dr. Aurora, published in 2006 in *Headache*, which details a study conducted in 10 subjects with migraine and 10 subjects with no history of migraine, migraineurs experienced, to varying degrees, paralysis of the muscles of the stomach, or gastroparesis. Dr. Aurora reported that this gastroparesis can result in up to an 80% slower rate of digestion, or gastric motility, in migraineurs. We believe that reduced gastric motility experienced by migraineurs during a migraine may result in low and inconsistent absorption of oral medications and is one of a variety of factors that may cause patients to fail to respond consistently to such medications.

Treatment of Acute Migraine

The FDA has approved acute migraine prescription medications in four classes:

Triptans, including a triptan combination;
Ergotamines (including dihydroergotamine, or DHE);
Analgesic combinations; and
A non-steroidal anti-inflammatory drug, or NSAID, which commercially launched in June 2010.

Currently, triptans constitute the most prescribed class of medication for the treatment of acute migraine in the U.S. Sumatriptan, approved by the FDA in 1992, is the most prescribed triptan, according to IMS.

The following table summarizes U.S. unit and dollar sales information for 2010, by product class, for prescription products indicated for the treatment of acute migraine, based on IMS data:

Product Class	**Key Product Brands (Drug)**	**Route of Administration**	**2010 Units Sold(1) (% Total)**	**2010 Sales (% Total)**
Triptan	Generic sumatriptan and Imitrex Maxalt (rizatriptan) Zomig (zolmitriptan) Relpax (eletriptan) Treximet (sumatriptan/naproxen) Sumavel DosePro (subcutaneous sumatriptan)	Tablet, orally disintegrating tablet, nasal spray, injection	123.1 million (74.5%)	$1.63 billion (96.6%)
Analgesic Combination	Epidrin, Midrin, Migrazone and generics (isometheptene mucate, dichloralphenazone, acetaminophen) Prodrin *(*acetaminophen, caffeine, isometheptene)	Capsule	37.3 million (22.6%)	$17.5 million (1.0%)
Ergotamine	Migranal (dihydroergotamine) DHE-45 and generics (dihydroergotamine) Cafergot and generics (dihydroergotamine, caffeine)	Nasal spray, injection, tablet suppository	4.8 million (2.9%)	$40.7 million (2.4%)

(1) A unit represents a single dose of each medication.

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As of December 31, 2010, there were seven commercially available triptan medications in the U.S. utilizing a variety of routes of administration: tablet, orally disintegrating tablet, nasal spray and injection. According to IMS, oral triptans, in tablet and orally disintegrating tablet formulations, accounted for 96% of triptan units sold in the U.S. in 2010, while non-oral triptans, in nasal spray and injectable formulations, accounted for only 4% of such triptan units.

Limitations of Current Treatments for Acute Migraine

We believe that most marketed migraine therapies are subject to significant limitations, including:

Administration challenges from nausea and vomiting. Patients with nausea often delay taking medication until the nausea subsides, may skip treatment altogether or, in extreme cases, force themselves to vomit. According to a survey conducted by the National Headache Foundation in 2008, 48% of respondents who ever experienced nausea or vomiting with a migraine reported that the nausea or vomiting had a moderate to major impact on when or how they take migraine medications. In the same survey, some migraineurs reported they delay taking migraine medication until nausea subsides, while others reported they avoid taking their migraine medication altogether because of nausea or vomiting. This runs contrary to well-accepted clinical practice, which stresses the importance of treating migraines without delay.

Poor or inconsistent relief. According to a 2001 article by Dr. Michel Ferrari published in *The Lancet*, a peer-reviewed medical journal, clinical trials have demonstrated that at least 40% of migraineurs fail to respond consistently to oral triptans. Based on data from multiple published third party clinical trials, including those described in a 2005 article by Dr. David Dodick published in *Headache*, we believe patients failure to respond consistently results from a variety of causes, including low and inconsistent absorption of oral medication because of reduced gastric motility.

Fear of adverse events. Many patients avoid or delay treatment because they fear adverse events, including triptan adverse events. Triptan adverse events include chest tightness, chest heaviness, numbness of the extremities, paresthesias, or tingling, and panic. According to U.S. prescribing information, the incidence of triptan adverse events is 47% for injection and up to 14% for oral sumatriptan. According to a 2003 article by Dr. R. Michael Gallagher published in *Headache*, 67% of migraine patients who use prescription migraine medication reported that they had delayed or avoided taking a prescription migraine medication due to concerns about adverse events.

As a result of these limitations, we believe that many migraineurs are dissatisfied with currently marketed medications. According to an article by Dr. Marcelo Bigal published in 2007 in *Headache*, over 80% of patients currently using a triptan have used a different triptan in the past and over 48% have used two or more different triptans or different formulations of the same triptan in the past. Bigal also reported that 79% of migraineurs stated that they would try a new medication.

Our Solution: Zelrix

We designed Zelrix specifically to overcome these limitations. Zelrix is an active, single-use sumatriptan transdermal patch that is applied during a migraine. Zelrix provides controlled delivery of sumatriptan through a non-oral route of administration. This approach is consistent with the AAN guidelines that recommend non-oral therapies for migraineurs who experience nausea or vomiting as significant migraine symptoms.

Zelrix Design

Zelrix utilizes SmartRelief, our proprietary transdermal delivery technology. SmartRelief uses a mild electrical current to actively deliver medication through the skin in a process called iontophoresis. To use Zelrix, a patient applies the patch to the upper arm or thigh and presses a button. Zelrix actively delivers sumatriptan for four hours. The patient may remove the patch whenever convenient after the dosing period.

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Potential Benefits of Zelrix

We believe that Zelrix overcomes the limitations of currently marketed migraine medications by:

Circumventing nausea and vomiting. Because Zelrix is administered transdermally, we believe that it will be an attractive treatment option for migraineurs suffering from nausea or vomiting who might otherwise delay or avoid taking medication.

Increasing consistency of response. Because Zelrix does not depend on gastrointestinal absorption, we believe that its absorption will not be compromised by reduced gastric motility experienced by some migraineurs. As a result, we believe that Zelrix will provide more consistent relief than oral medications.

Minimizing triptan adverse events. By tightly controlling the delivery of sumatriptan, Zelrix is designed to deliver sumatriptan plasma levels without exceeding levels that were associated with an increased prevalence of triptan adverse events reported by subjects treated with oral and injectable sumatriptan in our clinical trials. Because Zelrix tightly controls the delivery of sumatriptan, we believe that Zelrix use will result in a low incidence of triptan adverse events while effectively treating migraine as demonstrated in our clinical trials.

Patches have been used in the U.S. for decades for the transdermal delivery of various medications for a wide variety of indications, including nicotine addiction, birth control and pain relief. Because of the potential benefits of Zelrix and the familiarity of physicians and patients with patches, we believe that this route of administration of medication will be readily accepted by migraineurs.

Our Zelrix Development Program

We submitted an NDA for Zelrix to the FDA in October 2010 under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, or FDCA. The NDA is supported by Phase III clinical data in which Zelrix was evaluated in 796 patients and 8,913 migraines. In addition to our Zelrix data, under Section 505(b)(2), our NDA submission is based on existing published data and the FDA s previous finding of the safety and effectiveness of Imitrex.

Our clinical trial program for Zelrix consists of:

Eight Phase I clinical trials;

One pivotal Phase III clinical trial; and

Two long-term, open label Phase III trials, one of which has been completed and the other is expected to be completed in August 2011; and

One skin irritation study.

We established the primary and key secondary efficacy endpoints for our pivotal Phase III clinical trial for Zelrix based on discussions with the FDA. We believe, also based on our discussions with the FDA, that we are not required to conduct a second pivotal Phase III clinical trial for Zelrix. Also, because Zelrix will be applied to the skin, the FDA may require that we conduct a skin sensitization study. However, based on discussions with the FDA, we believe that the skin sensitization data being collected during our two long-term, open label Phase III trials has the potential to be sufficient, subject to review by the FDA as part of the Zelrix NDA, without the need to conduct a separate skin sensitization study.

Pivotal Phase III Clinical Trial

Our pivotal Phase III clinical trial for Zelrix was a randomized, double-blind, placebo-controlled trial designed to compare the safety and efficacy of Zelrix to an active transdermal placebo patch in patients with acute migraine. The inclusion criteria for the trial required that, in the three months prior to being randomized into the trial, patients generally had experienced moderate to severe pain during a migraine, had experienced migraines for at least one year and had reported from one to six migraines per month. Patients remained in the trial until they treated one migraine with a patch or two months after randomization into the trial, whichever occurred first.

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The primary efficacy endpoint for the trial was the proportion of patients treated with Zelrix who were headache pain free at two hours after patch application compared to patients treated with placebo. Using a standard migraine diary, patients rated their baseline headache pain severity immediately prior to applying a patch using a four-point scale, with zero for no pain, one for mild pain, two for moderate pain and three for severe pain. Patients applied a patch only if they rated their baseline headache pain severity as a two (moderate) or three (severe). Patients also rated the presence or absence of nausea, photophobia and phonophobia immediately prior to applying a patch. After patch application, patients recorded headache pain severity and presence or absence of nausea, photophobia and phonophobia at 0.5, 1, 2, 3, 4, 6, 12 and 24 hours.

Pivotal trials for all previously FDA approved triptans have used pain relief, which means reduction from severe or moderate pain to mild or no pain, as a primary efficacy endpoint. We believe pain free, which required the patient to record zero (none) with respect to headache pain severity, is a more exacting standard than pain relief.

The key secondary endpoints for our pivotal Phase III clinical trial were:

- The proportion of patients treated with Zelrix who were nausea free at two hours after patch application compared to patients treated with placebo;
- The proportion of patients treated with Zelrix who were photophobia free at two hours after patch application compared to patients treated with placebo; and
- The proportion of patients treated with Zelrix who were phonophobia free at two hours after patch application compared to patients treated with placebo.

Safety assessments in the trial included:

- Adverse event assessments;
- Investigator skin irritation examination scores; and
- Subject skin irritation self-examination scores.

In this trial, we treated 469 patients at 38 investigative sites in the U.S. The patient demographics of this trial were similar to those reported in other large scale migraine clinical trials. The Zelrix patient population included 197 women and 37 men. The placebo patient population included 201 women and 34 men. Each patient population had a mean age of approximately 41 years. We completed this trial in July 2009. Zelrix met each of the primary and key secondary endpoints with statistical significance. The following table summarizes the analysis of the primary endpoint, headache pain free at two hours and selected secondary endpoints:

ITT Analysis (1)		**Zelrix Patients**		**Placebo Patients**			
Symptom Two Hours After Patch Application	**LOCF (2)**	**226 Total**	**%**	**228 Total**	**%**	**% Difference**	**p value (3)**
Headache pain free		40	17.7%	21	9.2%	8.5%	0.0092
Headache pain relief		119	52.9	65	28.6	24.3	<0.0001
Nausea free		189	83.6	144	63.2	20.4	<0.0001
Photophobia free		116	51.3	83	36.4	14.9	0.0028
Phonophobia free		125	55.3	89	39.0	16.3	0.0002

(1) Intent-to-Treat (ITT) Analysis: Patients are analyzed in the groups to which they were randomized, regardless of whether they received or adhered to the allocated treatment. ITT analysis provides unbiased comparisons among the treatment groups and is the primary statistical analysis used by the FDA.

(2) Last Observation Carried Forward: Last observation carried forward is a method to address missing data. For each individual, missing values are replaced by the last observed value of that variable.

(3) The results of a clinical trial are statistically significant if they are unlikely to have occurred by chance. We determined the statistical significance of the trial results based on a widely used, conventional statistical method

that establishes the *p* value of the results. The FDA requires a *p* value of 0.05 or less to demonstrate statistical significance.

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In addition to achieving statistically significant results for the primary and key secondary endpoints, Zelrix also demonstrated statistically significant results for a number of other secondary endpoints, including:

Headache pain relief within one hour. Zelrix demonstrated statistically significant headache pain relief at one hour after patch application, with 29% of Zelrix patients experiencing headache pain relief as compared to 19% of placebo patients *(p = 0.0123)*. While not statistically significant, 38% more Zelrix patients than placebo patients experienced pain relief in 30 minutes, 29 of 226 Zelrix patients compared to 21 of 228 placebo patients.

Sustained pain relief. In a retrospective analysis we conducted, for those patients who experienced pain relief at two hours, Zelrix demonstrated statistically significant sustained pain relief at each measurement point from two hours through 24 hours after patch application, with 34% of Zelrix patients experiencing sustained pain relief as compared to 21% of placebo patients *(p = 0.0015)*. For purposes of this analysis, we defined patients with sustained relief as patients with no pain or mild pain at all measurement points from two hours through 24 hours after patch application and who had not taken rescue medication.

Freedom from nausea within one hour. Zelrix demonstrated statistically significant freedom from nausea at one hour after patch application, with 71% of Zelrix patients being nausea free as compared to 58% of placebo patients *(p = 0.0251)*.

Freedom from migraine. Zelrix demonstrated statistically significant freedom from migraine at two hours after patch application, with 16% of Zelrix patients being migraine free as compared to 8% of placebo patients *(p = 0.0135)*. Freedom from migraine means the absence of headache, nausea, photophobia and phonophobia.

Decreased use of rescue medication. Zelrix demonstrated a statistically significant difference in the number of patients that used pain or nausea rescue medication during the 24 hours after patch application, with 40% of Zelrix patients using rescue medication as compared to 60% of placebo patients *(p <0.0001)*. Rescue medications are any additional medications taken by the patient to relieve symptoms of migraine after patch application.

A total of 117 patients, or 50% of patients, receiving Zelrix and 103 patients, or 44% of patients, receiving the placebo patch experienced at least one treatment-emergent adverse event, which is an event that was not present prior to patch application or a worsening of either the intensity or frequency of a symptom following patch application. The most common adverse events reported in the trial among patients receiving Zelrix related to the application site and included application site pain and application site tingling. There were no deaths or serious adverse events in this trial. Zelrix demonstrated skin tolerability typical of other transdermal products, with mild to moderate redness generally present upon patch removal.

Patients receiving Zelrix exhibited a low incidence of triptan adverse events, with 1.7% experiencing atypical sensations and 1.7% experiencing pain and other pressure sensations. Patients described all of these adverse events to be of mild intensity, except for one adverse event, which a patient described as cold sensation head of moderate intensity.

Long-Term, Open Label Phase III Trials

We have completed one long-term, open label Phase III trial and have a second which we expect to complete in August 2011. These trials evaluate the safety of Zelrix in the treatment of acute migraine over 12 months. Patient eligibility requirements in these trials are similar to the requirements for our completed pivotal Phase III clinical trial. As of December 31, 2010, Zelrix has been evaluated in 662 patients in these trials.

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Phase I Clinical Trials

We have completed eight Phase I clinical trials of Zelrix. In four of these Phase I clinical trials, we evaluated Zelrix prototypes and design characteristics in healthy adult subjects to establish proof of concept. In the fifth Phase I clinical trial, we compared the pharmacokinetics of Zelrix to oral Imitrex in patients with migraine. Pharmacokinetics refers to a drug s absorption, distribution and metabolism in, and excretion from, the body and measures, among other things, bioavailability of a drug, or concentration of drug in the plasma.

In the sixth Phase I clinical trial, we compared the pharmacokinetics of Zelrix to three routes of administration of Imitrex in healthy adult subjects: 20 mg nasal spray, 100 mg tablet and 6 mg injection. As intended, treatment with Zelrix resulted in sumatriptan plasma levels between the levels of 20 mg Imitrex nasal spray and the 100 mg Imitrex oral tablet. After Zelrix application, sumatriptan absorption in plasma reached therapeutic levels within 30 minutes. In addition, in this trial, treatment with Zelrix resulted in less variability in sumatriptan plasma levels than either 100 mg oral tablet or 20 mg nasal spray formulations, supporting our belief that transdermal administration provides more predictable delivery by bypassing absorption through the gastrointestinal system.

At the time of patch removal, more than 75% of subjects had no or minimal skin redness, and within 48 hours following patch removal, all subjects had no or minimal skin redness. We also evaluated adverse events by different routes of administration. The trial categorized adverse events as either Atypical Sensations or Pain and Pressure Sensations. The following table sets forth each of these adverse events by category for each route of administration:

Summary of Triptan Adverse Events

		Number of Subjects Reporting Event (%)			
Adverse Event		Zelrix (17	Nasal Spray (23	Injection (23	Oral (23
Categorization	Preferred Term	Subjects)	Subjects)	Subjects)	Subjects)
Atypical Sensation	Any adverse events			14 (60.9%)	2 (8.7%)
	Burning sensation mucosal			3 (13.0%)	
	Ear discomfort			1 (4.3%)	
	Facial pain			1 (4.3%)	
	Feeling hot			2 (8.7%)	
	Flushing			6 (26.1%)	
	Head discomfort			1 (4.3%)	1 (4.3%)
	Hot flush			3 (13.0%)	1 (4.3%)
	Sensation of heaviness			1 (4.3%)	
	Sensation of pressure			1 (4.3%)	
Pain and Pressure Sensation	Any adverse events			2 (8.7%)	4 (17.4%)
	Neck pain				2 (8.7%)
	Sensation of heaviness			1 (4.3%)	1 (4.3%)
	Sensation of pressure			1 (4.3%)	1 (4.3%)

In subjects treated with oral and injectable sumatriptan, all of the triptan adverse events occurred in subjects with sumatriptan plasma levels exceeding 50 nanograms per milliliter. In this trial, the maximum sumatriptan plasma level observed for subjects receiving Zelrix reached therapeutic levels, but did not exceed 50 nanograms per milliliter. We believe the ability of Zelrix to control sumatriptan plasma levels within this dosing range explains why subjects receiving Zelrix in this trial did not experience triptan adverse events.

The seventh Phase I clinical trial compared the pharmacokinetics of Zelrix in 8 healthy elderly volunteers to 24 healthy young adult volunteers and the pharmacokinetics of Zelrix applied to the upper arm and applied to the thigh. The results from this study demonstrated no clinically significant difference in the pharmacokinetic profile of Zelrix

based upon age or application site.

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The eighth Phase I clinical trial was a confirmatory bioavailability study in which pharmacokinetic analysis was conducted in 30 healthy adult subjects. This trial was successfully completed and the data included in our NDA.

Skin Irritation Study

In order to evaluate the skin irritation profile of Zelrix, we measured the amount of skin irritation resulting from repeated application of Zelrix in 10 healthy adult subjects. This study was successfully completed and the data included in our NDA.

Commercial Strategy

If Zelrix is approved by the FDA, we plan to build a commercial infrastructure to launch Zelrix in the U.S., including a specialty sales force of approximately 100 people. We expect to direct our marketing efforts at high potential prescribers of Zelrix, primarily consisting of neurologists and headache specialists. We believe a sales force of this size will enable us to address a significant portion of the commercial opportunity for Zelrix. We may seek to further penetrate the U.S. market in the future by expanding our sales force or through collaborations with other pharmaceutical or biotechnology companies. This would enable us to target additional physicians who are high prescribers of migraine medications.

Once we establish our commercial infrastructure, we may acquire additional products to market and sell or collaborate with pharmaceutical or biotechnology companies to market and sell their products using our sales force. We may also seek to commercialize Zelrix outside the U.S., although we currently plan to do so only with a collaborator.

Pipeline Products

In addition to migraine, we also seek to identify other market opportunities in central nervous system disorders for which improved medication delivery can address significant medical needs. Our current research and development pipeline consists of two preclinical product candidates, one for the treatment of Parkinson s disease and one for the treatment of schizophrenia and bipolar disorder.

NP201: Product candidate for the continuous symptomatic treatment of Parkinson s disease

Parkinson s disease is a progressive, degenerative disease characterized by movement symptoms such as tremor or trembling in the hands, arms, and legs; rigidity of the limbs and trunk; slowness of movement; and impaired balance and coordination. According to the Parkinson s Disease Foundation, Parkinson s disease affects about one million people in the U.S. and more than four million people worldwide. Although symptoms of Parkinson s disease can appear at any age, the average age of onset is 60.

The loss of neurons in the brain that help to control movement causes Parkinson s disease. These neurons produce dopamine, a neurotransmitter that transmits signals that control movement. Currently, no cure exists for Parkinson s disease. Symptomatic treatments rely on the replacement of dopamine through either levodopa, which the brain converts to dopamine, or dopamine agonists, which mimic dopamine.

Multiple challenges complicate the treatment of Parkinson s disease. Intermittent dosing of oral medications leads to periods of on after dosing and periods of off as the medication wears off. During on periods, excessive levels o medication can produce adverse events, primarily abnormal movements. During off periods, low levels of medication lead to poor efficacy. In addition, Parkinson s disease is a progressive disease, which causes patients to become less responsive to their medication over time and more sensitive to excessive drug levels.

The majority of Parkinson s disease patients currently use oral medications that require administration one to three times per day, exposing the patient to varying medication levels. The intermittent dosing of oral medications further complicates treatment, as patients experience periods of on after dosing and periods of off as the medication wears off. According to a 2009 article by Dr. Fabrizio Stocchi published in *Parkinsonism and Related Disorders*, a peer-reviewed medical journal, experts believe that intermittent dosing may result in more frequent and serious adverse events and may hasten the progression of Parkinson s disease by causing harm to the remaining dopamine receptors. As Dr. Stocchi reported, studies suggest that continuous medication delivery can alleviate the symptoms of Parkinson s disease without inducing the abnormal movements caused by too much medication.

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Only two Parkinson s disease medications currently provide for continuous delivery, and neither is approved in the U.S. Duodopa is a levodopa/carbidopa gel marketed by Abbott Laboratories that requires the surgical insertion of a tube into the patient s small intestine. APO-go is an injectable apomorphine marketed by Britannia Pharmaceuticals Limited that requires the patient to wear a pump around his or her waist. Because both APO-go and Duodopa are difficult to administer, they are generally reserved for complicated and difficult to control patients.

We designed NP201 to provide continuous delivery of Parkinson s disease medication in an easy to administer and tolerable dose formulation. NP201 consists of our LAD technology combined with ropinirole, a generic, FDA approved dopamine agonist also known as Requip. After administration, NP201 is designed to slowly dissolve while releasing ropinirole.

We have studied NP201 in several animal models. We believe the data from these studies suggest that NP201 can provide continuous, stable medication levels for up to two months. In addition, we completed a proof of concept study in a well-accepted animal model of Parkinson s disease that we believe suggests NP201 has the potential to provide continuous symptomatic relief for up to two months per dose and to significantly decrease the incidence of adverse events associated with current treatments.

In March 2010, we met with the FDA to discuss our development plan for NP201. Based on this meeting, we believe that we can submit an NDA for NP201 under Section 505(b)(2) of the FDCA and that the FDA will require only a single successful pivotal Phase III clinical trial for approval. We initiated an acute toxicology study for NP201 in the fourth quarter of 2010 and plan to submit an Investigational New Drug Application, or IND, in the first half of 2011.

NP202: Product candidate for the long-term treatment of schizophrenia and bipolar disorder

Schizophrenia is a life-long serious psychiatric illness that causes people to lose touch with reality and often interferes with their ability to think clearly, manage emotions, make decisions and relate to others. Bipolar disorder, or manic depression, is another life-long psychiatric illness that causes extreme shifts in mood, energy and functioning. These changes may be subtle or dramatic and typically vary greatly over the course of a person s life as well as among individuals.

According the National Alliance on Mental Illness, schizophrenia affects over two million adults in the U.S., while bipolar disorder affects over ten million adults in the U.S. According to an article by Dr. Eric Wu published in 2005 in *The Journal of Clinical Psychiatry*, a peer-reviewed medical journal, as of 2002 the estimated direct healthcare costs of schizophrenia in the U.S. were $22.7 billion, including outpatient care, medications and long-term care.

Patient compliance with medication has been a long-standing problem in the treatment of schizophrenia. As reported in an article by Dr. Jeffrey Lieberman published in 2005 in *The New England Journal of Medicine*, a peer-reviewed medical journal, the Clinical Antipsychotic Trials in Intervention Effectiveness, or CATIE, study, conducted between 2001 and 2004, indicated that 74% of schizophrenia patients become non-compliant with their medication within 18 months of commencing the use of medication. According to an article by Patricia Thieda published in 2003 in *Psychiatric Services*, a peer-reviewed medical journal, schizophrenia patients with poor compliance are more than twice as likely to experience relapse than patients with good compliance. We believe medication compliance represents a significant opportunity for improved treatments.

In an attempt to improve patient compliance, physicians administer antipsychotic drugs through depot injections. Depot injections release medication over a longer period than conventional injections or oral medications. Depot injection products include Risperdal Consta and Invega Sustenna, both marketed by Johnson & Johnson, and Zyprexa Relprew, marketed by Eli Lilly & Co. These drugs provide two to four weeks of therapy per dose.

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We believe that NP202 potentially could provide a significant improvement over existing treatment options for patients suffering from schizophrenia or bipolar disorder because:

- We are developing NP202 to provide up to three months of continuous delivery of an atypical antipsychotic with a single dose. Currently available products provide therapy for only two to four weeks, resulting in frequent physician visits and increasing the risk of non-compliance;
- We are designing NP202 to allow a physician to remove the implant at any time during the dosing period. With currently available injectable products, physicians and patients cannot stop therapy, which may discourage some physicians and patients concerned about adverse events; and
- We are developing NP202 as an easy to administer, pre-loaded injectable product that can be stored at room temperature. Risperdal Consta, the leading depot injectable product, must be prepared and mixed prior to administration.

We have developed NP202 prototype products, initiated pre-IND activities and plan to submit an IND to the FDA in 2012.

Our Proprietary Delivery Technologies

Our current drug development activities use two proprietary medication delivery technologies: SmartRelief and LAD. Zelrix incorporates SmartRelief, while NP201 and NP202 both incorporate LAD. We have exclusive worldwide rights to both technologies.

SmartRelief Technology

SmartRelief is our proprietary transdermal medication delivery technology based on iontophoresis, a non-invasive method of actively transporting molecules, such as sumatriptan, that are not able to be delivered passively through the skin. Iontophoresis involves the application of a mild electrical current to the skin through two reservoirs. One reservoir contains ionized, or charged, medication. The other reservoir contains a counter ion, commonly sodium chloride, or salt. When a current is applied, medication molecules travel out of the reservoir into the skin, where blood vessels absorb and disburse them throughout the body.

Unlike passive transdermal technologies, which rely on diffusion for medication delivery, iontophoresis controls the amount and rate of medication delivery. Iontophoresis enables transdermal delivery of a variety of medications that cannot be delivered passively through the skin. It is possible to deliver a variety of different medications, including proteins and peptides, using iontophoresis. The FDA has approved two pharmaceutical products incorporating iontophoresis, Johnson & Johnson s IONSYS system and Vyteris, Inc. s LidoSite topical system for analgesia, and multiple iontophoretic medical devices.

Long-Acting Delivery Technology

We designed LAD to improve the control, consistency and convenience of medication delivery. LAD is comprised of a biodegradable polymer matrix using commonly available medical polymers and an active drug, combined to form a small implant for injection just below the skin. We also have designed LAD to allow a physician to remove it using a minor surgical procedure if a decision is made to stop therapy.

To date, we have tested several neuropsychiatric compounds formulated with LAD in multiple animal models. Based on these studies, we believe LAD has the potential to treat patients for one to three months with a single dose of a therapy. As a result, we believe LAD has the potential, depending upon the indication, to improve one or more of efficacy, medication compliance and incidence of adverse events. We have not yet tested LAD in humans.

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Manufacturing

We currently have no manufacturing facilities and limited personnel with manufacturing experience. We currently use, and expect to depend on, third party contract manufacturers to manufacture Zelrix and our other product candidates for our preclinical and clinical needs and, if we obtain marketing approval for our product candidates, for commercial supply. We believe our reliance on contract manufacturing helps us control our expenses, as the construction, maintenance and insurance of pharmaceutical manufacturing facilities requires significant capital.

We have established an internal quality control and quality assurance program, including a set of standard operating procedures and specifications consistent with current Good Manufacturing Practices, or cGMP. The cGMP requirements govern quality control of the manufacturing process and documentation policies and procedures. We depend on our third party contract manufacturers for continued compliance with cGMP requirements.

Multiple pharmaceutical manufacturers produce sumatriptan, the active ingredient in Zelrix. We currently purchase sumatriptan from two suppliers and the various components of SmartRelief from multiple manufacturers, all on a purchase order basis.

Under the terms of a development and license agreement that we entered into in September 2007, LTS Lohmann Therapie-Systeme AG, or LTS, manufactures Zelrix. We pay fees to LTS for manufacturing development, preparation of manufacturing documentation for our Zelrix NDA, manufacture of our clinical supplies and preparation for commercial manufacturing. We expect to enter into a commercial manufacturing agreement for Zelrix with LTS. To that end, in June 2010, we entered into an equipment funding agreement with LTS, under which we agreed to fund the purchase by LTS of the machinery that LTS will use to produce the commercial supply of Zelrix, if we enter into a commercial manufacturing agreement. The machinery is customized to the particular manufacturing specifications of Zelrix.

We purchase preclinical supplies of NP201, consisting of LAD and the active ingredient, ropinirole, from SurModics Pharmaceuticals, Inc., or SurModics. Ropinirole is generic and available from multiple sources.

Competition

The pharmaceutical and biotechnology industries are intensely competitive and subject to rapid and significant technological change. Our major competitors include organizations such as major multinational pharmaceutical companies, established biotechnology companies and specialty pharmaceutical and generic drug companies. Many of our competitors have greater financial and other resources than we have, such as larger research and development staffs and more extensive marketing and manufacturing organizations. As a result, these companies may obtain marketing approval more rapidly than we are able and may be more effective in selling and marketing their products. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Our competitors may succeed in developing, acquiring or licensing on an exclusive basis technologies and drug products that are more effective or less costly than Zelrix or any other product candidate that we are currently developing or that we may develop, which could render our products obsolete and noncompetitive. We expect any products that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third party payors. We also expect to face competition in our efforts to identify appropriate collaborators or partners to help commercialize our product candidates in our target commercial markets.

We anticipate Zelrix will compete with currently marketed triptans, including Imitrex (sumatriptan), Maxalt (rizatriptan), Zomig (zolmitriptan), Relpax (eletriptan), Axert (almotriptan), Frova (frovatriptan), Amerge (naratriptan), Treximet (sumatriptan/naproxen) and Sumavel DosePro (sumatriptan). In addition, we anticipate competition from generic sumatriptan, the active ingredient in Imitrex, and generic versions of other branded triptans that have lost or will lose their patent exclusivity. For example, Amerge, the branded version of naratriptan, lost patent protection in July 2010. In addition, we expect other triptan patents to expire between 2012 and 2025. Many of these products are manufactured and marketed by large pharmaceutical companies and are well accepted by physicians, patients and third party payors. Because of the low cost, health insurers may require or encourage use of, and consumers may use, a generic triptan prior to trying Zelrix. If approved, Zelrix will also compete with other currently

approved products, including analgesic combinations, NSAIDs and ergotamines (including DHE).

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If approved, we believe that Zelrix s features, including its convenient, non-oral route of administration, controlled delivery of medication and consistent dosing, will differentiate it from existing migraine treatments, particularly for migraineurs suffering from nausea or vomiting.

In addition to marketed migraine medications, both large and small companies have migraine product candidates in various stages of clinical development. These include Merck & Co., Inc. s telcagepant, an orally administered calcitonin gene related peptide antagonist, and Levadex from MAP Pharmaceuticals, Inc., an inhaled formulation of DHE, both for acute migraine. Each of these has either completed or is in Phase III clinical development. Additionally, MAP has entered into a collaboration with Allergan Inc., whose Botox product was approved for the treatment of chronic migraine in October 2010. Pursuant to the collaboration, the parties will co-promote Levadex following its potential FDA approval.

Our strategy to compete in the migraine market includes:

- Elevating physician awareness of current treatment limitations and impact on patients;
- Emphasizing differentiating features of Zelrix; and
- Building on physician experience with sumatriptan, the most prescribed migraine medication.

As with Zelrix, if approved, each of NP201 and NP202 will face competition from generic and branded products. Specifically, NP201 will face competition from generic immediate release and extended release versions of ropinirole and the dopamine agonist pramiprexole, as well as from two continuous delivery medications, a levadopa gel and an injectable apomorphine. NP202 will face competition from a variety of branded and generic versions of antipsychotic medications, in addition to several other sustained delivery depot formulations of atypical antipsychotics.

License, Development and Commercial Agreements

Our material license, development and commercial agreements are described below.

Travanti Pharma Inc.

In July 2008, we entered into an asset purchase and license agreement with Travanti Pharma Inc., or Travanti, pursuant to which we acquired from Travanti a patent application, including all supporting documentation and priority documents, that is directed to transdermal delivery of anti-migraine medications using an active delivery patch. Under the agreement, we granted Travanti a nonexclusive, royalty-free, perpetual, worldwide license to use the purchased patent application, and the invention covered by such patent application, outside the field of migraine. In May 2009, Teikoku Pharma USA, Inc. acquired Travanti.

In addition, under the Travanti agreement, we obtained a perpetual, worldwide, exclusive, royalty-free license, with the right to grant sublicenses, under Travanti s patent rights, including issued U.S. Patent No. 6,745,071, as described in more detail under Intellectual Property and Exclusivity, and know-how that relate generally to specified iontophoresis technology to develop, make and commercialize migraine products. If we make improvements that directly relate to such Travanti patents and patent applications, Travanti will hold a nonexclusive, royalty-free, perpetual, worldwide license to use such improvements outside the field of migraine. The Travanti agreement does not contain any termination provisions under which our license rights would terminate.

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LTS Lohmann Therapie-Systeme AG

In September 2007, we entered into a development and license agreement with LTS, which was amended as of April 2008, February 2009 and May 2010. Under the development and license agreement, LTS agreed to perform development activities relating to Zelrix in accordance with an agreed upon development plan and to use commercially reasonable efforts to provide us with supplies for our clinical trials. LTS also has provided us with supplies for our non-clinical use.

Pursuant to the terms of the development and license agreement, each party exclusively owns any inventions related to such party s existing intellectual property that arise out of the development program. The parties jointly own any joint inventions that arise out of the development program not solely based on one party s existing intellectual property. Each party grants to the other a non-exclusive, royalty-free license under its respective intellectual property for the sole purpose of developing Zelrix. If we execute a commercial manufacturing agreement for Zelrix with LTS, LTS will have the exclusive right to manufacture Zelrix and LTS will grant us an exclusive, worldwide, royalty-free license under LTS s intellectual property to use, import, sell, market and distribute, or have imported, sold, marketed or distributed, Zelrix. If we do not execute a commercial manufacturing agreement with LTS, we may not have access to LTS s proprietary technology and know-how necessary to develop, manufacture or commercialize Zelrix.

The development and license agreement remains in effect until the parties execute a commercial manufacturing agreement or until either party terminates the agreement by its terms. We may terminate the development and license agreement at any time upon 60 days notice to LTS. In addition, either party may terminate the agreement if the other party materially breaches the agreement and fails to cure the breach during a 60-day cure period. Either party may terminate the agreement if the development committee established under the agreement determines that it is not feasible to develop a product as anticipated under the development plan.

In June 2010, we entered into an equipment funding agreement with LTS under which we agreed to fund the purchase by LTS of manufacturing equipment for Zelrix and LTS agreed to purchase and install the equipment according to an agreed upon project plan. We will fund the purchase of the equipment by making 14 monthly installment payments to LTS, in the aggregate amount of 5.4 million. The monthly installment payments commenced in June 2010. As of December 31, 2010, 2.7 million, or approximately $3.6 million based on exchange rates as of December 31, 2010, remains to be paid in the remaining monthly installments. We expect that the installation, validation and qualification of all of the equipment will be completed prior to our anticipated commercial launch of Zelrix in the first half of 2012. LTS will own the purchased equipment and will be responsible for its routine and scheduled maintenance and repair. However, during the term of the LTS development and license agreement or any subsequent commercial manufacturing agreement that the parties may enter into, LTS will be required to use the purchased equipment solely for fulfilling its obligations to manufacture Zelrix. In addition, during the term of the development and license agreement or such commercial manufacturing agreement, LTS is prohibited from encumbering the purchased equipment and may not sell or dispose of such equipment, except that LTS may transfer ownership of it to its affiliate, LTS Lohmann Therapy Systems Partnership L.P. Moreover, if we do not enter into a commercial manufacturing agreement with LTS or if we terminate the equipment funding agreement due to a breach by LTS, LTS must, at its option, either transfer ownership of the equipment to us or refund to us the purchase price of the equipment, less depreciation.

The equipment funding agreement will remain in effect until the later of the completion by LTS of all installation activities or the execution of a commercial manufacturing agreement.

University of Pennsylvania

We entered into a patent license agreement with the University of Pennsylvania, or Penn, which became effective in July 2006 and was amended in May 2007. Under the patent license agreement, Penn granted to us exclusive, worldwide rights under specified Penn patent applications, and patents issuing therefrom, to make, use and sell products using LAD. Under the agreement, we have the right to sublicense, subject to specified conditions, including the payment of sublicense fees.

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The patent license agreement requires that we use commercially reasonable efforts to develop and commercialize licensed products. We must submit development plans annually for products we intend to develop. We must also commit at least $250,000 annually towards the development and commercialization of licensed products, until the first commercial sale of the first licensed product.

Under the patent license agreement, we pay Penn annual license maintenance fees of up to $50,000 until the first commercial sale of the first licensed product. The agreement currently covers NP201 and NP202. In addition, we have agreed to pay Penn aggregate milestone payments of up to $950,000 upon the achievement of specified development and regulatory milestones related to each licensed product that contains ropinirole or other specified active ingredients, including the active ingredients in NP201 and NP202, and royalties in the low single digits on worldwide net sales of such licensed products. We and Penn have agreed to negotiate the milestone payments and royalties payable for each licensed product that contains an active ingredient other than those currently specified in the agreement. If we grant a sublicense of our rights under the Penn patent rights to a third party, we must pay Penn a specified portion of certain income received from such third party sublicensee.

The patent license agreement, and our obligation to pay royalties to Penn, will terminate, on a product by product basis, on the later of the expiration or abandonment of the last Penn patent, which we expect will occur in April 2027, or ten years after the first commercial sale of a licensed product if no patent issues from the patent applications licensed from Penn under the agreement. We may terminate the agreement at any time upon 60 days notice to Penn. Penn may terminate the agreement in connection with our uncured breach, bankruptcy or insolvency.

SurModics Pharmaceuticals, Inc.

In March 2007, we entered into a feasibility evaluation agreement with SurModics (formerly known as Brookwood Pharmaceuticals, Inc.), which was amended in December 2007, April 2008, July 2008, October 2008, March 2009 and May 2010. Under the feasibility evaluation agreement, we and SurModics, from time to time, enter into plans of work whereby SurModics performs evaluation, development and formulation work for NP201 and provides us with preclinical supplies of NP201.

Pursuant to the feasibility evaluation agreement, each party owns exclusively any inventions arising out of the development program if they are based solely on that party s existing intellectual property. Any inventions under the development program based on both parties intellectual property are jointly owned. SurModics has the right to practice aspects of joint research inventions developed under the feasibility agreement that do not relate to our product or use our technology or confidential information. We received an option to obtain an exclusive, royalty bearing license under SurModics technology and intellectual property necessary to make, have made, use and sell NP201. We agreed to pay SurModics for its services and supplies on a time and materials basis. The feasibility evaluation agreement will remain effective until mutually agreed upon by the parties or until terminated by us upon at least two weeks advanced written notice to SurModics.

In September 2009, upon our exercise of the option under the feasibility evaluation agreement, we entered into a license agreement with SurModics, pursuant to which we received an exclusive worldwide license, with the right to sublicense, under SurModics intellectual property, including its interest in joint inventions developed under the feasibility agreement, to make, have made, use, sell, import and export products covered by the license agreement, comprised of a biodegradable, preformed, macroscopic implant device consisting of ropinirole, as the sole active pharmaceutical ingredient, incorporated into the controlled delivery system developed or optimized under the feasibility agreement. The license agreement currently covers NP201. We granted SurModics an exclusive, perpetual, worldwide, royalty-free license under our interest in joint inventions for uses that do not relate to products covered by the license agreement or include any of our existing technology or confidential information. We also granted SurModics a right of first negotiation to manufacture clinical supplies of covered products. If we and SurModics enter into such clinical manufacturing agreement, SurModics has a right of first negotiation to manufacture commercial supplies of covered products.

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Under the license agreement, we have agreed to pay SurModics aggregate milestone payments of up to $4.75 million upon the first achievement of specified development, regulatory and sales level milestones related to the first clinical indication approved by a regulatory authority for covered products. We must also pay an additional milestone payment upon regulatory approval of each additional clinical indication for covered products and royalties in the low single digits on worldwide net sales of commercial product. In countries where a valid SurModics patent claim does not cover the product, the applicable royalty rate decreases. If we do not enter into a commercial manufacturing agreement with SurModics, the applicable royalty rate will increase, though it will remain in the low single digits.

Under the license agreement we are responsible for developing and obtaining regulatory approval for covered products. We have agreed to use commercially reasonable efforts to actively develop and obtain regulatory approvals to market a covered product, including NP201, in major markets throughout the world. In addition, we have agreed to comply with specific diligence milestones to obtain such regulatory approval and to develop and commercialize a covered product in the U.S.

The license agreement and our obligation to pay SurModics royalties will terminate on a country by country basis on the later of the date on which a valid SurModics patent claim no longer covers the product or an agreed period after the first commercial sale of the product in such country. Thereafter the license will become an exclusive, perpetual fully paid-up license.

We have the right to terminate the license agreement for any reason at any time upon ninety days notice to SurModics. Either party has the right to terminate the agreement in connection with the other party s uncured material breach, bankruptcy or insolvency. SurModics may either terminate the license agreement or make it non-exclusive if we fail to meet the agreed upon diligence milestones or otherwise fail to use commercially reasonable efforts to develop and obtain regulatory approval for a covered product.

Intellectual Property and Exclusivity

We seek to protect our product candidates and our technology through a combination of patents, trade secrets, proprietary know-how, FDA exclusivity and contractual restrictions on disclosure.

Patents and Patent Applications

Our policy is to seek to protect the proprietary position of our product candidates by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business. U.S. patents generally have a term of 20 years from the date of nonprovisional filing. Because patent protection is not available for the active pharmaceutical ingredient compounds included in our current product candidates, we will need to rely primarily on the protections afforded by device, formulation and method of use patents.

As of December 31, 2010, we exclusively license one issued U.S. patent and its foreign counterparts, and own five U.S. patent applications, as well as corresponding Patent Cooperation Treaty, or PCT, applications and their foreign counterparts, which relate to Zelrix.

Our licensed issued U.S. Patent No. 6,745,071, owned by Travanti, is generally directed towards wearable iontophoretic devices, including Zelrix, that are prepackaged as complete self-contained units that include an active pharmaceutical ingredient to be administered, a provision for isolating moisture sources from the electrodes and from the power source during storage to optimize shelf stability, and a simple, user-friendly mechanism to transfer the active pharmaceutical ingredient and counter ion reservoirs to the electrodes. The expiration date for this patent is in 2023. There are corresponding patents in Australia, Canada and Korea which will also expire in 2023 and corresponding patent applications pending in certain other countries which will expire in 2023 if issued. Under the Travanti asset purchase and license agreement, we also have a perpetual, worldwide, exclusive, royalty-free license, in the field of migraine, to Travanti patents, patent applications and know-how that relate generally to iontophoresis.

Our five U.S. pending patent applications are generally directed to:

- Methods and devices for treating migraine using integrated iontophoretic patches, including Zelrix;
- Active ingredient reservoir formulations, including the Zelrix formulation; and
- Electronic control systems and methods for use of the same in delivering an active pharmaceutical ingredient for an integrated iontophoretic patch, including Zelrix.

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All of the U.S. applications currently have pending international applications, as well as corresponding foreign patent applications in certain select countries. If the five U.S. applications and their foreign corresponding applications issue, we generally expect these patents to expire between 2027 and 2030.

Additionally, as of December 31, 2010, we own or exclusively license one issued U.S. patent and eight U.S. patent applications, as well as corresponding PCT patent applications and their foreign counterparts, relating to our LAD pipeline product candidates. The U.S. patent, and eight non-provisional U.S. applications and their corresponding foreign applications, if issued, are generally expected to expire between 2021 and 2030. These patents and patent applications include claims generally directed to the LAD technology, as well as the use of the LAD technology in conjunction with various medications in the treatment of certain neurological and psychiatric diseases, including Parkinson s disease, schizophrenia and bipolar disorder.

Under the LTS development and license agreement and the SurModics license agreement, we have rights to LTS s and SurModics proprietary processing and manufacturing technologies related to our product candidates.

FDA Marketing Exclusivity

The FDA may grant three years of marketing exclusivity in the U.S. for the approval of new and supplemental NDAs, including Section 505(b)(2) NDAs, for, among other things, new indications, dosages or dosage forms of an existing drug, if new clinical investigations that were conducted or sponsored by the applicant are essential to the approval of the application. Additionally, six months of marketing exclusivity in the U.S. is available under Section 505A of the FDCA if, in response to a written request from the FDA, a sponsor submits and the agency accepts requested information relating to the use of the approved drug in the pediatric population. This six month pediatric exclusivity period is not a standalone exclusivity period, but rather is added to any existing patent or non-patent exclusivity period for which the drug product is eligible. Based on our clinical trial program for Zelrix, we plan to seek three years of marketing exclusivity upon receipt of FDA approval for Zelrix. We may also seek an additional period of six months exclusivity from the FDA if the FDA requests, and we successfully complete, pediatric clinical trials for Zelrix.

Trade Secrets and Proprietary Information

We seek to protect our proprietary information, including our trade secrets and proprietary know-how, by requiring our employees, consultants and other advisors to execute confidentiality agreements upon the commencement of their employment or engagement. These agreements generally provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not be disclosed to third parties except in specific circumstances. In the case of our employees, the agreements also typically provide that all inventions resulting from work performed for us, utilizing our property or relating to our business and conceived or completed during employment shall be our exclusive property to the extent permitted by law. Where appropriate, agreements we obtain with our consultants also typically contain similar assignment of invention obligations. Further, we require confidentiality agreements from entities that receive our confidential data or materials.

Government Regulation

Federal Food, Drug and Cosmetic Act

Prescription drug products are subject to extensive pre- and post-market regulation by the FDA, including regulations that govern the testing, manufacturing, distribution, safety, efficacy, approval, labeling, storage, record keeping, reporting, advertising and promotion of such products under the FDCA, and its implementing regulations, and by comparable agencies and laws in foreign countries. Failure to comply with applicable FDA or other regulatory requirements may result in civil or criminal penalties, recall or seizure of products, partial or total suspension of production or withdrawal of the product from the market. The FDA must approve any new unapproved drug or dosage form, including a new use of a previously approved drug, prior to marketing in the U.S. All applications for FDA approval must contain, among other things, information relating to safety and efficacy, pharmaceutical formulation, stability, manufacturing, processing, packaging, labeling and quality control.

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New Drug Applications

Generally, the FDA must approve any new drug before marketing of the drug occurs in the U.S. This process generally involves:

- Completion of preclinical laboratory and animal testing in compliance with the FDA s Good Laboratory Practice, or GLP, regulations;
- Submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin in the U.S.;
- Performance of human clinical trials, including adequate and well-controlled clinical trials, to establish the safety and efficacy of the proposed drug product for each intended use;
- Satisfactory completion of an FDA pre-approval inspection of the product s manufacturing facility or facilities to assess compliance with the FDA s cGMP regulations; and
- Submission to, and approval by, the FDA of an NDA application.

The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that the FDA will grant approvals for any of our product candidates on a timely basis, if at all. Preclinical tests include laboratory evaluation of product chemistry, formulation and stability, as well as studies to evaluate toxicity in animals. The results of preclinical tests, together with manufacturing information and analytical data, comprise a part of an IND application submission to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial, including concerns regarding exposure of human research subjects to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Our submission of an IND may not result in FDA authorization to commence a clinical trial. In addition, the FDA requires a separate submission to an existing IND for each successive clinical trial conducted during product development. Further, an independent institutional review board, or IRB, covering each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that center and it must monitor the clinical trial until completed. The FDA, the IRB or the sponsor may suspend a clinical trial at any time, or from time to time, on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk. As a separate amendment to an IND, a sponsor may submit a request for a special protocol assessment, or SPA, from the FDA. Under the SPA procedure, a sponsor may seek the FDA s agreement on the design, conduct and analyses of, among other things, a clinical trial intended to form the primary basis of an efficacy claim. If the FDA agrees in writing, it may not change its agreement after the clinical trial begins, except in limited circumstances, such as upon identification of a substantial scientific issue essential to determining the safety and effectiveness of a product candidate after commencement of a Phase III clinical trial. If the clinical trial succeeds, the sponsor can ordinarily rely on it as the primary basis for approval with respect to effectiveness. Clinical testing also must satisfy extensive Good Clinical Practice, or GCP, regulations, including regulations for informed consent, IRB review and approval and IND submission.

For purposes of an NDA submission and approval, typically, the conduct of human clinical trials occurs in the following three pre-market sequential phases, which may overlap:

- *Phase I:* Sponsors initially conduct clinical trials in a limited population to test the product candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients, such as cancer patients.
- *Phase II:* Sponsors conduct clinical trials generally in a limited patient population to identify possible adverse effects and safety risks, to determine the efficacy of the product for specific targeted indications and to determine dose tolerance and optimal dosage. Sponsors may conduct multiple Phase II clinical trials to obtain information prior to beginning larger and more extensive Phase III clinical trials.
- *Phase III:* These include expanded controlled and uncontrolled trials, including pivotal clinical trials. When Phase II evaluations suggest the effectiveness of a dose range of the product and acceptability of such product s safety profile, sponsors undertake Phase III clinical trials in larger patient populations to obtain additional information needed to evaluate the overall benefit and risk balance of the drug and to provide an adequate basis to develop labeling.

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In addition, sponsors may conduct Phase IV clinical trials after the FDA approves a drug. In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor s agreement to conduct additional clinical trials to further assess the drug s safety or effectiveness after NDA approval. Such post approval trials are typically referred to as Phase IV clinical trials.

Sponsors submit the results of product development, preclinical studies and clinical trials to the FDA as part of an NDA. NDAs must also contain extensive manufacturing information and proposed labeling. Upon receipt, the FDA initially reviews the NDA to determine whether it is sufficiently complete to initiate a substantive review. If the FDA identifies deficiencies that would preclude substantive review, the FDA will refuse to accept the NDA and will inform the sponsor of the deficiencies that must be corrected prior to resubmission. If the FDA accepts the submission for substantive review, the FDA typically reviews the NDA in accordance with established time frames. Under the Prescription Drug User Fee Act, or PDUFA, the FDA agrees to specific goals for NDA review time through a two-tiered classification system, Priority Review and Standard Review. For a Priority Review application, the FDA aims to complete the initial review cycle in six months. Standard Review applies to all applications that are not eligible for Priority Review. The FDA aims to complete Standard Review NDAs within a ten-month timeframe. Our Zelrix NDA is being reviewed by the FDA under Standard Review and we anticipate that any NDA that we may file for our other product candidates would receive Standard Review. Review processes often extend significantly beyond anticipated completion dates due to FDA requests for additional information or clarification, difficulties scheduling an advisory committee meeting or FDA workload issues. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to the application s approval. The recommendations of an advisory committee do not bind the FDA, but the FDA generally follows such recommendations.

If an NDA does not satisfy applicable regulatory criteria, the FDA may deny approval of an NDA or may require, among other things, additional clinical data or an additional pivotal Phase III clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we do. The FDA could also require a risk evaluation and mitigation strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, a commitment to conduct one or more post-market studies or clinical trials and the correction of identified manufacturing deficiencies, including the development of adequate controls and specifications.

After approval, the NDA sponsor must comply with comprehensive requirements governing, among other things, manufacturing, marketing activities, distribution, annual reporting and adverse event reporting. If new safety issues are identified following approval, the FDA can require the NDA sponsor to revise the approved labeling to reflect the new safety information; conduct post-market studies or clinical trials to assess the new safety information; and implement a REMS program to mitigate newly-identified risks. In addition, if after approval the FDA determines that the product does not meet applicable regulatory requirements or poses unacceptable safety risks, the FDA may take other regulatory actions, including requesting a product recall or initiating suspension or withdrawal of the NDA approval.

Drugs may be marketed only for approved indications and in accordance with the provisions of the approved label. Further, if we modify a drug, including any changes in indications, labeling or manufacturing processes or facilities, the FDA may required us to submit and obtain FDA approval of a new or supplemental NDA, which may require us to develop additional data or conduct additional preclinical studies and clinical trials.

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Under PDUFA, NDA applicants must pay significant NDA user fees upon submission. In addition, manufacturers of approved prescription drug products must pay annual establishment and product user fees.

Section 505(b)(2) New Drug Applications

As an alternate path to FDA approval, particularly for modifications to drug products previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, and permits the submission 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. The FDA interprets Section 505(b)(2) of the FDCA to permit the applicant to rely upon the FDA s previous findings of safety and effectiveness for an approved product. The FDA may also require companies to perform additional clinical trials or measurements to support any change from the previously approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that a Section 505(b)(2) NDA relies on clinical trials conducted for a previously approved drug product or the FDA s prior findings of safety and effectiveness for a previously approved drug product, the 505(b)(2) applicant must submit patent certifications in its 505(b)(2) application with respect to any patents listed for the approved product on which the application relies in the FDA s publication, Approved Drug Products with Therapeutic Equivalence Evaluations, commonly referred to as the Orange Book. Specifically, the applicant must certify for each listed patent that (1) the required patent information has not been filed; (2) the listed patent has expired; (3) the listed patent has not expired, but will expire on a particular date and approval is not sought until after patent expiration; or (4) the listed patent is invalid, unenforceable or will not be infringed by the proposed new product. A certification that the new product will not infringe the previously approved product s listed patent or that such patent is invalid or unenforceable is known as a Paragraph IV certification. If the applicant does not challenge one or more listed patents through a Paragraph IV certification, the FDA will not approve the Section 505(b)(2) NDA application until all the unchallenged listed patents claiming the referenced product have expired. Further, the FDA will also not accept or approve, as applicable, a Section 505(b)(2) NDA application until any non-patent exclusivity, such as exclusivity for obtaining approval of a New Chemical Entity, listed in the Orange Book for the referenced product, has expired.

If the 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the owner of the referenced NDA for the previously approved product and relevant patent holders within 20 days after the 505(b)(2) NDA has been accepted for submission by the FDA. The NDA and patent holders may then initiate a patent infringement suit against the 505(b)(2) applicant. Under the FDCA, the filing of a patent infringement lawsuit within 45 days of receipt of the notification regarding a Paragraph IV certification automatically prevents the FDA from approving the Section 505(b)(2) NDA for 30 months, or until a court deems the patent unenforceable, invalid or not infringed, whichever is earlier. Moreover, in cases where a 505(b)(2) application containing a Paragraph IV certification is submitted during a previously approved drug s five year exclusivity period, the 30-month period is automatically extended to prevent approval of the 505(b)(2) application until the date that is seven and one-half years after approval of the previously approved reference product. The court also has the ability to shorten or lengthen either the 30 month or the seven and one-half year period if either party is found not to be reasonably cooperating in expediting the litigation. Thus, the Section 505(b)(2) applicant may invest a significant amount of time and expense in the development of its product only to be subject to significant delay and patent litigation before its product may be commercialized. Alternatively, if the NDA applicant or relevant patent holder does not file a patent infringement lawsuit within the specified 45 day period, the 30 month stay will not prevent approval of the 505(b)(2) application.

Notwithstanding the approval of many products by the FDA pursuant to Section 505(b)(2), over the last few years, some pharmaceutical companies and others have objected to the FDA s interpretation of Section 505(b)(2). If the FDA changes its interpretation of Section 505(b)(2), or if the FDA s interpretation is successfully challenged in court, this could delay or even prevent the FDA from approving our NDA for Zelrix or any other Section 505(b)(2) NDA that we submit.

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In the NDA submissions for our product candidates, we intend to follow the development and approval pathway permitted under the FDCA that we believe will maximize the commercial opportunities for these product candidates.

International Regulation

In addition to regulations in the U.S., we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of any future products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

For example, under European Union, or EU, regulatory systems, sponsors may submit marketing authorizations either under a centralized or mutual recognition procedure. Under the centralized procedure, a single application to the European Medicines Agency, or the EMEA, leads to an approval granted by the European Commission which permits the marketing of a product throughout the EU. The centralized procedure is mandatory for certain classes of medicinal products, but optional for others. For example, all medicinal products developed by certain biotechnological means, and those developed for cancer and other specified diseases and disorders including neurodegenerative disorders, must be authorized via the centralized procedure. The national procedure is used for products that are not required to be authorized by the centralized procedure. Under the national procedure, an application for a marketing authorization is submitted to the competent authority of one member state of the EU. The holders of a national marketing authorization may submit further applications to the competent authorities of the remaining member states via either the decentralized or mutual recognition procedure. The decentralized procedure enables applicants to submit an identical application to the competent authorities of all member states where approval is sought at the same time as the first application, while under the mutual recognition procedure, products are authorized initially in one member state, and other member states where approval is sought are then requested to recognize the original authorization based upon an assessment report prepared by the original authorizing competent authority. Both the decentralized and mutual recognition procedures should take no longer than 90 days, but if one member state makes an objection, which under the legislation can only be based on a possible risk to human health, the application will be automatically referred to the Committee for Medicinal Products for Human Use, or the CHMP, of the EMEA. If a referral for arbitration is made, the procedure is suspended. However, member states that have already approved the application may, at the request of the applicant, authorize the product in question without waiting for the result of the arbitration. Such authorizations will be without prejudice to the outcome of the arbitration. For all other concerned member states, the opinion of the CHMP, which is binding, could support or reject the objection or alternatively could reach a compromise position acceptable to all EU countries concerned. The arbitration procedure may take an additional year before a final decision is reached and may require the delivery of additional data.

As with FDA approval we may not be able to secure regulatory approvals in Europe in a timely manner, if at all. Additionally, as in the U.S., post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution, would apply to any product that is approved in Europe, and failure to comply with such obligations could have a material adverse effect on our ability to successfully commercialize any product.

The conduct of clinical trials in the EU is governed by the European Clinical Trials Directive (2001/20/EC), which was implemented in May 2004. This directive governs how regulatory bodies in member states control clinical trials. No clinical trial may be started without a clinical trial authorization granted by the national competent authority and favorable ethics approval. Accordingly, there is a marked degree of change and uncertainty both in the regulation of clinical trials and in respect of marketing authorizations which face us for our products in Europe.

In addition to regulations in Europe and the U.S., we will be subject to a variety of foreign regulations governing clinical trials and commercial distribution of any future products.

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Third Party Payor Coverage and Reimbursement

Although none of our product candidates have been commercialized for any indication, if the FDA approves these products for marketing, commercial success of our product candidates will depend, in part, upon the availability of coverage and reimbursement from third party payors at the federal, state and private levels. Government payor programs, including Medicare and Medicaid, private health care insurance companies and managed care plans have attempted to control costs by limiting coverage and the amount of reimbursement for particular procedures or drug treatments. The United States Congress and state legislatures from time to time propose and adopt initiatives aimed at cost containment, which could impact our ability to sell our products profitably.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act and the associated reconciliation bill, which we refer to collectively as the Health Care Reform Law, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Health Care Reform Law revises the definition of average manufacturer price for reporting purposes, which could increase the amount of Medicaid drug rebates to states once the provision is effective. Further, beginning in 2011, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may require us to modify our business practices with healthcare practitioners. We will not know the full effects of the Health Care Reform Law until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the effect of the Health Care Reform Law, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Moreover, in the coming years, additional changes could be made to governmental healthcare programs that could significantly impact the success of our products.

The cost of pharmaceuticals continues to generate substantial governmental and third party payor interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Our results of operations could be adversely affected by current and future healthcare reforms.

Some third party payors also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers that use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our product candidates and operate profitably.

Manufacturing Requirements

We and our third party manufacturers must comply with applicable FDA regulations relating to FDA s cGMP regulations. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our products must meet cGMP requirements to the satisfaction of the FDA pursuant to a pre-approval inspection before we can use them to manufacture our products. We and our third party manufacturers are also subject to periodic inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations. Failure to comply with statutory and regulatory requirements subjects a manufacturer to possible legal or regulatory action, including warning letters, the seizure or recall of products, injunctions, consent decrees placing significant restrictions on or suspending manufacturing operations and civil and criminal penalties. Adverse experiences with the product must be reported to the FDA and could result in the imposition of market restrictions through labeling changes or in product removal. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product occur following approval.

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Other Regulatory Requirements

With respect to post-market product advertising and promotion, the FDA imposes a number of complex regulations on entities that advertise and promote pharmaceuticals, which include, among other things, standards for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. The FDA has very broad enforcement authority under the FDCA, and failure to abide by these regulations can result in penalties, including the issuance of a warning letter directing entities to correct deviations from FDA standards, a requirement that future advertising and promotional materials be pre-cleared by the FDA, civil money penalties and state and federal civil and criminal investigations and prosecutions.

We are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, government agencies have broad regulatory and enforcement powers, including the ability to levy fines and civil penalties.

In addition, drug manufacturers also are subject to federal and state requirements and restrictions concerning interactions with physicians and other healthcare professionals, internal compliance programs, and transparency reporting requirements, including, for example, reporting of physician payments and other transfers of value, reporting of physician ownership or investment interests, reporting of marketing expenditures and clinical trial registration and reporting of clinical trial results on the publicly available clinical trial databank maintained by the National Institutes of Health at www.ClinicalTrials.gov.

Employees

As of December 31, 2010, we employed 26 full-time employees, of which 16 were engaged in research and development and clinical trials and 10 were engaged in administration, finance, marketing, business development and legal. None of our employees is represented by a labor union. Generally, our employees are at-will employees. However, we have entered into employment agreements with certain of our executive officers.

Available Information

We maintain a website at www.nupathe.com. We make available free of charge through our website s Investor Relations SEC Filings page most of our filings with the SEC, including our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to such reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended. These materials are available as soon as reasonably practicable after they are filed with or furnished to the SEC. The public can also obtain materials that we file with the SEC through the SEC s website at http://www.sec.gov or at the SEC s Public Reference Room at 100F Street, NE, Washington, DC 20549. Information on the operation of the Public Reference Room is available by calling the SEC at 800-SEC-0330.

Also available through our website s Investor Relations Corporate Governance page are charters for the Audit, Compensation and Nominating and Corporate Governance Committees of the Company s Board of Directors, the Company s Corporate Governance Guidelines and the Company s Code of Business Conduct and Ethics.

The references to our website and the SEC s website are intended to be inactive textual references only. Neither the contents of our website, nor the contents of the SEC s website, are incorporated by reference herein.

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ITEM 1A. RISK FACTORS

Our business is subject to substantial risks and uncertainties. Any of the risks and uncertainties described below, either alone or taken together, could materially and adversely affect our business, financial condition, results of operations or prospects. In addition, these risks and uncertainties could cause actual results to differ materially from those expressed or implied by forward-looking statements contained in this Form 10-K (please read the Cautionary Note Regarding Forward-Looking Statements appearing at the beginning of this Form 10-K). The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial may also materially and adversely affect our business, financial condition, results of operations or prospects and could cause actual results to differ materially from those expressed or implied by forward-looking statements.

Risks Related to Development and Commercialization of Our Product Candidates

We are heavily dependent on the success of Zelrix. If we fail to obtain marketing approval for and commercialize Zelrix, or experience delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the development of our most advanced product candidate, Zelrix. Zelrix is the only product candidate for which we have conducted clinical trials, and to date we have not marketed, distributed or sold any products. Our ability to generate revenues in the near term is substantially dependent on our ability to develop and commercialize Zelrix. On October 29, 2010, we submitted an NDA to the FDA seeking approval to commercialize Zelrix for treatment of acute migraine. We cannot commercialize Zelrix prior to obtaining FDA approval. Even though Zelrix has completed its pivotal Phase III clinical trial with positive results and we have submitted an NDA, Zelrix is still, nonetheless, susceptible to the risks of failure inherent at any stage of drug development, including the appearance of unexpected adverse events, manufacturing and testing failures, and the FDA s determination Zelrix is not approvable. As a company, we have never obtained marketing approval for or commercialized a drug. It is possible that the FDA may review our data and conclude that our application is insufficient to obtain marketing approval of Zelrix. The FDA may require that we conduct additional clinical or preclinical trials or manufacture additional validation batches before it will consider our application. If the FDA requires additional studies or data, we would incur increased costs and delays in the marketing approval process, which may require us to expend more resources than we have available. In addition, the FDA may not consider sufficient any additional required trials that we perform and complete.

Even if we believe that the data from our clinical trials support marketing approval of Zelrix in the U.S., the FDA may not agree with our analysis and may not approve our NDA. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing Zelrix, generating revenues and achieving profitability.

The commercial success of Zelrix and any other product candidates that we develop, if approved in the future, will depend upon significant market acceptance of these products among physicians, patients and third party payors.

As a company, we have never commercialized a product candidate for any indication. Even if any product candidate that we develop, including Zelrix, is approved by the appropriate regulatory authorities for marketing and sale, it may not gain acceptance among physicians, patients and third party payors. If our products for which we obtain marketing approval do not gain an adequate level of acceptance, we may not generate significant product revenues or become profitable. Market acceptance of Zelrix, and any other product candidates that we develop, by physicians, patients and third party payors will depend on a number of factors, some of which are beyond our control, including:

- The efficacy, safety and other potential advantages in relation to alternative treatments;
- The relative convenience and ease of administration;
- The availability of adequate coverage or reimbursement by third parties, such as insurance companies and other healthcare payors, and by government healthcare programs, including Medicare and Medicaid;

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The prevalence and severity of adverse events;

The cost of treatment in relation to alternative treatments, including generic products;

The extent and strength of marketing and distribution support;

The limitations or warnings contained in a product s FDA approved labeling; and

Distribution and use restrictions imposed by the FDA or to which we agree as part of a mandatory risk evaluation and mitigation strategy or voluntary risk management plan.

For example, even if the medical community accepts that Zelrix is safe and effective for its approved indications, physicians and patients may not immediately be receptive to Zelrix and may be slow to adopt it as an accepted treatment for acute migraine. In addition, even though we believe Zelrix has significant advantages, because no head-to-head trials comparing Zelrix to competing products have been conducted, it is unlikely that any labeling approved by the FDA will contain claims that Zelrix is safer or more effective than competitive products or will permit us to promote Zelrix as being superior to competing products. Further, the availability of numerous inexpensive generic forms of migraine therapy products may also limit acceptance of Zelrix among physicians, patients and third party payors. If Zelrix is approved but does not achieve an adequate level of acceptance among physicians, patients and third party payors, we may not generate meaningful revenues from Zelrix and we may not become profitable.

It will be difficult for us to profitably sell any of our product candidates that the FDA approves, including Zelrix, if reimbursement for such product candidate is limited.

Market acceptance and sales of Zelrix or any other product candidates that we develop will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and these third party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that reimbursement will be available for Zelrix or any other product candidates that we develop and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, our products for which we obtain marketing approval. Numerous generic products may be available at lower prices than branded therapy products, such as Zelrix, if it is approved, which may also reduce the likelihood and level of reimbursement for our product candidates, including Zelrix. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize Zelrix or any other product candidates that we develop. The active ingredient in Zelrix, sumatriptan, is available as a generic. Because of the low cost, health insurers may require or encourage use of, and consumers may use, a generic triptan prior to trying Zelrix.

If we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates after they are approved, we may be unable to generate product revenues.

We currently do not have a commercial infrastructure for the marketing, sales and distribution of pharmaceutical products. In order to commercialize our products, we must build our marketing, sales and distribution capabilities or make arrangements with third parties to perform these services. If Zelrix is approved by the FDA, we plan to build a commercial infrastructure to launch Zelrix in the U.S., including a specialty sales force of approximately 100 people. We may seek to further penetrate the U.S. market in the future by expanding our sales force or through collaborations with other pharmaceutical or biotechnology companies. We may also seek to commercialize Zelrix outside the U.S., although we currently plan to do so only with a collaborator.

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The establishment and development of our own sales force and related compliance plans to market any products we may develop will be expensive and time consuming and could delay any product launch, and we may not be able to successfully develop this capability. We, or our future collaborators, will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. In the event we are unable to develop a marketing and sales infrastructure, we would not be able to commercialize Zelrix or any other product candidates that we develop, which would limit our ability to generate product revenues.

Companies such as ours often expand their sales force and marketing capabilities for a product prior to it being approved by the FDA so that the drug can be commercialized upon approval. Although our plan is to hire our sales representatives and most of our other sales and marketing personnel only if Zelrix is approved by the FDA, we will incur expenses prior to product launch in recruiting this sales force and developing a marketing and sales infrastructure. If the commercial launch of Zelrix is delayed as a result of FDA requirements or other reasons, we would incur these expenses prior to being able to realize any revenue from product sales. Even if we are able to effectively hire a sales force and develop a marketing and sales infrastructure, our sales force and marketing teams may not be successful in commercializing Zelrix or any other product candidates that we develop.

To the extent we rely on third parties to commercialize any products for which we obtain marketing approval, we may receive less revenues than if we commercialized these products ourselves. In addition, we would have less control over the sales efforts of any other third parties involved in our commercialization efforts. In the event we are unable to collaborate with a third party marketing and sales organization, our ability to generate product revenues may be limited either in the U.S. or internationally.

We face significant competition from other pharmaceutical and biotechnology companies. Our operating results will suffer if we fail to compete effectively.

The pharmaceutical and biotechnology industries are intensely competitive and subject to rapid and significant technological change. Our major competitors include organizations such as major multinational pharmaceutical companies, established biotechnology companies and specialty pharmaceutical and generic drug companies. Many of our competitors have greater financial and other resources than we have, such as larger research and development staff and more extensive marketing and manufacturing organizations. As a result, these companies may obtain marketing approval more rapidly than we are able to and may be more effective in selling and marketing their products. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Our competitors may succeed in developing, acquiring or licensing on an exclusive basis technologies and drug products that are more effective or less costly than Zelrix or any other drug candidate that we are currently developing or that we may develop, which could render our products obsolete and noncompetitive. We expect any products that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third party payors. We also expect to face competition in our efforts to identify appropriate collaborators or partners to help commercialize our product candidates in our target commercial markets.

The competition in the market for acute migraine medication is intense. The majority of marketed prescription products for treatment of acute migraine in the U.S. are in the triptan class in tablet, orally-disintegrating tablet, nasal spray and injectable therapies. The largest selling triptan in units is sumatriptan, with approximately 70.5 million individual units sold in the U.S. in 2010, including approximately 10.2 million units attributable to GlaxoSmithKline plc s (GSK), branded sumatriptan products, Imitrex and Treximet. There are at least six other branded triptan therapies being sold by pharmaceutical and biotechnology companies, including Maxalt from Merck & Co., Inc. (Merck), the largest selling triptan with sales of approximately $496.0 million in the U.S. in 2010. In June 2010, the FDA approved King Pharmaceuticals, Inc. s Alsuma subcutaneous sumatriptan injection

If approved, Zelrix will face competition from inexpensive generic versions of sumatriptan and generic versions of other branded products of competitors that have lost or will lose their patent exclusivity, including the largest selling triptan, Maxalt, which is expected to lose patent exclusivity between 2012 and 2014. In addition, we expect other triptan patents to expire between 2013 and 2017. Many of these products are manufactured and marketed by large pharmaceutical companies and are well accepted by physicians, patients and third party payors. Because of the low

cost, health insurers likely would require or encourage use of, and consumers likely would use, a generic triptan prior to trying Zelrix.

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In addition to marketed migraine medications, if approved, Zelrix may face competition from migraine product candidates in various stages of clinical development by both large and small companies. These include Merck s telcagepant, an orally administered calcitonin gene related peptide antagonist, and Levadex from MAP Pharmaceuticals, Inc., an inhaled formulation of dihydroergotamine, both for acute migraine. Each of these has either completed or is in Phase III clinical development. Additionally, MAP has entered into a collaboration with Allergan Inc., whose Botox product was approved for the treatment of chronic migraine in October 2010. Pursuant to the collaboration, the parties will co-promote Levadex following its potential FDA approval. Zelrix may also compete with other drug candidates in development for the treatment of migraine. If we are unable to demonstrate the advantages of Zelrix over competing drugs and drug candidates, we will not be able to successfully commercialize Zelrix and our results of operations will suffer.

As with Zelrix, if approved, each of NP201 and NP202 will face competition from generic and branded products. Specifically, NP201, a biodegradable, subcutaneous, injectable polymer implant combined with ropinirole, will face competition from generic immediate release and extended release versions of ropinirole and the dopamine agonist pramiprexole, as well as from two continuous delivery medications, a levadopa gel and an injectable apomorphine. NP202, a biodegradable, subcutaneous, injectable polymer implant combined with an atypical antipsychotic medication, will face competition from a variety of branded and generic versions of antipsychotic medications, in addition to several other sustained delivery depot formulations of atypical antipsychotics.

As a result of all of these factors, our competitors may succeed in obtaining patent protection or FDA approval or discovering, developing and commercializing migraine and other therapies before we do.

Any failure or delay in preclinical studies or clinical trials for our product candidates may cause us to incur additional costs or delay or prevent the commercialization of our product candidates and could severely harm our business.

Before obtaining marketing approval for the sale of our product candidates, we must conduct, at our own expense, extensive preclinical tests and then clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing, in particular, is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Even if preclinical studies and early phase clinical trials succeed, it is necessary to conduct additional clinical trials in larger numbers of subjects taking the medication for longer periods before seeking FDA approval to market and sell a medication in the U.S. Clinical data is often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain FDA approval for their products. A failure of one or more of our clinical trials can occur at any stage of testing.

We may experience numerous unforeseen events during, or as a result of, the clinical trial process, which could delay or prevent us from receiving marketing approval or commercializing our product candidates, including the following:

- Regulators or institutional review boards may not authorize us to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- Our clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or we may abandon projects that we expect to be promising;
- The number of subjects required for our clinical trials may be larger than we anticipate, enrollment in our clinical trials may be slower than we anticipate, or participants may drop out of our clinical trials at a higher rate than we anticipate;
- We might have to suspend or terminate our clinical trials if the participants are being exposed to unacceptable health risks;

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- Regulators or institutional review boards may require that we hold, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or our clinical protocols;
- Regulators may refuse to accept or consider data from clinical trials for various reasons, including noncompliance with regulatory requirements or our clinical protocols;
- The cost of our preclinical or clinical trials may be greater than we anticipate;
- The supply or quality of our product candidates or other materials necessary to conduct our clinical trials may be insufficient or inadequate; and
- The effects of our product candidates may not be the desired effects or the desired level of effect or may include undesirable side effects or the product candidates may have other unexpected characteristics.

A number of these risks remain applicable to our ongoing long-term, open label Phase III trial for Zelrix.

Although our only ongoing clinical trial for Zelrix is fully enrolled, we expect to undertake additional clinical trials in the future for Zelrix or our other product candidates. Subject enrollment, which is a significant factor in the timing of clinical trials, is affected by a variety of factors, including the following:

- The size and nature of the subject population;
- The proximity of subjects to clinical sites;
- The eligibility criteria for the trial;
- The design of the clinical trial;
- Competing clinical trials; and
- Clinicians and subjects perceptions as to the potential advantages of the medication being studied in relation to other available therapies, including any new medications that may be approved for the indications we are investigating.

Furthermore, we plan to rely on clinical trial sites to ensure the proper and timely conduct of our clinical trials, and while we have agreements governing their committed activities, we have limited influence over their actual performance. Any delays or unanticipated problems during clinical testing, such as enrollment in our clinical trials being slower than we anticipate or participants dropping out of our clinical trials at a higher rate than we anticipate, could increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenues.

Serious adverse events or other safety risks could require us to abandon development and preclude or limit approval of our product candidates.

We may voluntarily suspend or terminate our clinical trials if at any time we believe that they present an unacceptable risk to participants. In addition, regulatory agencies or institutional review boards may at any time order the temporary or permanent discontinuation of our clinical trials or of investigators in the clinical trials if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, or that they present an unacceptable safety risk to participants. If we elect or are forced to suspend or terminate a clinical trial of any product candidates, the commercial prospects of such product candidates will be harmed and our ability to generate product revenues from any of these product candidates, if at all, will be delayed or eliminated.

Clinical trials for our product candidates involve testing in large subject populations, which could reveal a high prevalence of adverse events. If these effects include undesirable serious adverse events or have unexpected characteristics, we may need to abandon our development of these product candidates. Alternatively, the identification of serious adverse events or other significant safety risks could result in the imposition of approval requirements, such as labeling or distribution and use restrictions that limit the available market for our product candidates.

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If we fail to acquire, develop and commercialize product candidates other than Zelrix, our prospects for future growth and our ability to sustain profitability may be limited.

A key element of our strategy is to develop and commercialize a portfolio of product candidates in addition to Zelrix. To do so, we plan to obtain additional product candidates or technologies primarily through acquisitions or licenses. We may not be successful in our efforts to identify and develop additional product candidates, and any product candidates we do identify may not produce commercially viable drugs that safely and effectively treat their indicated conditions. To date, our efforts have yielded two product candidates in addition to Zelrix, both of which are currently in preclinical development.

Our development programs may initially show promise in identifying potential product leads, yet fail to produce product candidates for clinical development. In addition, identifying new treatment needs and product candidates requires substantial technical, financial and human resources on our part. If we are unable to maintain or secure additional development program funding or continue to devote substantial technical and human resources to such programs, we may have to delay or abandon these programs. Any product candidate that we successfully identify may require substantial additional development efforts prior to commercial sale, including preclinical studies, extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are susceptible to the risks of failure that are inherent in pharmaceutical product development.

We may be unable to license or acquire suitable product candidates or technologies from third parties for a number of reasons. In particular, the licensing and acquisition of pharmaceutical products is competitive. A number of more established companies are also pursuing strategies to license or acquire products. These established companies may have a competitive advantage over us due to their size, cash resources or greater clinical development and commercialization capabilities. In addition, we expect competition in acquiring product candidates to increase, which may lead to fewer suitable acquisition opportunities for us as well as higher acquisition prices.

Other factors that may prevent us from licensing or otherwise acquiring suitable product candidates include the following:

- We may be unable to license or acquire the relevant technology on terms that would allow us to make an appropriate return from such product;
- Companies that perceive us to be their competitors may be unwilling to assign or license their product rights to us; or
- We may be unable to identify suitable products or product candidates within our areas of expertise.

Product liability lawsuits could divert our resources, result in substantial liabilities and reduce the commercial potential of any products that we may successfully develop.

The risk that we may be sued on product liability claims is inherent in the development of pharmaceutical products. We will face an even greater risk if we commercially sell any products that we develop. If we cannot successfully defend ourselves against claims that our product candidates, or any products we may commercialize, cause injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, these lawsuits may:

- Expose us to adverse publicity;
- Decrease demand for any products that we successfully develop;
- Cause clinical trial participants to withdraw from clinical trials or be reluctant to enroll;
- Divert our management from pursuing our business strategy;

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Increase warnings on our product label;

Be costly to defend; and

Force us to limit or forgo further development and commercialization of these products.

Although we maintain general liability and product liability insurance with limits, subject to deductibles, of $2.0 million in the aggregate for general liability, $1.0 million in the aggregate for umbrella liability coverage for payments that exceed the general liability limits and $2.0 million in the aggregate for product liability, this insurance may not fully cover potential liabilities. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial. In addition, inability to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims could prevent or inhibit the development and commercial production and sale of our products, which could adversely affect our business, operating results and financial condition.

A variety of risks associated with our planned international business relationships could materially adversely affect our business.

We may enter into agreements with third parties for the development and commercialization of Zelrix and possibly other products in international markets. If we do so, we would be subject to additional risks related to entering into international business relationships, including:

Differing regulatory requirements for drug approvals in foreign countries;

Potentially reduced protection for intellectual property rights;

The potential for so-called parallel importing, which is what happens when a local seller, faced with higher local prices, opts to import goods from a foreign market, with lower prices, rather than buying them locally;

Unexpected changes in tariffs, trade barriers and regulatory requirements;

Economic weakness, including inflation, or political instability in particular foreign economies and markets;

Compliance with tax, employment, immigration and labor laws for employees traveling abroad;

Foreign taxes;

Foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;

Workforce uncertainty in countries where labor unrest is more common than in the U.S.;

Production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

Business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, volcanoes, typhoons, floods, hurricanes and fires.

These and other risks may materially adversely affect our ability to attain or sustain profitable operations.

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Risks Related to Our Financial Condition and Capital Requirements

We have incurred significant operating losses since inception and anticipate that we will incur continued losses for the foreseeable future. We may never become profitable.

As of December 31, 2010, we had an accumulated deficit of approximately $79.8 million. We are a development stage specialty pharmaceutical company with no products approved for commercial sale and, to date, have not generated any revenues. We have funded our operations to date primarily with the proceeds of the sale of common stock, convertible preferred stock, preferred stock warrants, convertible notes and borrowings under debt facilities. We expect to continue to incur substantial additional operating losses for at least the next several years as we continue to develop our product candidates and seek marketing approval and, subject to obtaining such approval, the eventual commercialization of Zelrix and our other product candidates. In addition, we are incurring additional costs of operating as a public company and, if we obtain marketing approval for Zelrix, will incur significant sales, marketing and outsourced manufacturing expenses. As a result, we expect to continue to incur significant and increasing losses for the foreseeable future.

To achieve and maintain profitability, we need to generate significant revenues from future product sales. This will require us to be successful in a range of challenging activities, including:

- Obtaining marketing approval for the marketing of Zelrix and possibly other product candidates;
- Commercializing Zelrix and any other product candidates for which we obtain marketing approval; and
- Achieving market acceptance of Zelrix and any other product candidates for which we obtain marketing approval in the medical community and with patients and third party payors.

On October 29, 2010, we submitted an NDA for Zelrix to the FDA. Zelrix will require marketing approval and investment in commercial capabilities, including manufacturing and sales and marketing efforts, before its product sales generate any revenues for us. Because of the numerous risks and uncertainties associated with drug development and commercialization, we are unable to predict the extent of any future losses. We may never successfully commercialize any products, generate significant future revenues or achieve and sustain profitability.

If we fail to obtain additional financing, we may not be able to complete development of and commercialize Zelrix or any other product candidates.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to:

- seek marketing approval for Zelrix and complete any additional development activities that may be required by the FDA;
- Launch and commercialize Zelrix and any other product candidates for which we obtain marketing approval; and
- Continue our development programs to advance our internal product pipeline, which currently consists of two preclinical product candidates.

We will need substantial additional funding and may be unable to raise capital when needed or on attractive terms, which would force us to significantly delay, scale back or discontinue the development or commercialization of Zelrix or our other product candidates.

We believe that our existing cash and cash equivalents will be sufficient to fund our operations and capital requirements through FDA approval of Zelrix and into the expected commercial launch of Zelrix in the U.S. in the first half of 2012. However, changing circumstances may cause us to consume capital faster than we currently anticipate, and we may need to spend more money than currently expected because of such circumstances.

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Our future capital requirements will depend on many factors, including:

- The outcome of the FDA s review of the NDA for Zelrix;
- The cost, scope and timing of activities undertaken to prepare for the potential commercialization of Zelrix;
- The extent to which the FDA may require us to perform additional clinical trials for Zelrix;
- The cost of purchasing manufacturing and other capital equipment for our potential products;
- The scope, progress, results and costs of development for our other product candidates;
- The extent to which we acquire or invest in new products, businesses and technologies; and
- The extent to which we choose to establish collaboration, co-promotion, distribution or other similar agreements for product candidates.

To the extent that our capital resources are insufficient to meet our future operating and capital requirements, we will need to finance our cash needs through public or private equity offerings, debt financings, corporate collaboration and licensing arrangements or other financing alternatives. The covenants under the May 2010 Loan Facility and the pledge of our assets as collateral limit our ability to obtain additional debt financing. We have no committed external sources of funds. Additional equity or debt financing or corporate collaboration and licensing arrangements may not be available on acceptable terms, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will be prevented from pursuing acquisition, licensing, development and commercialization efforts and our ability to generate revenues and achieve or sustain profitability will be substantially harmed.

If we raise additional funds by issuing equity securities, our stockholders will experience dilution. Debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any debt financing or additional equity that we raise may contain terms, such as liquidation and other preferences, which are not favorable to us or our stockholders. If we raise additional funds through collaboration and licensing arrangements with third parties, it may be necessary to relinquish valuable rights to our technologies, future revenue streams or product candidates or to grant licenses on terms that may not be favorable to us.

Our indebtedness may limit cash flow available to invest in the ongoing needs of our business.

As of December 31, 2010, we had $5.0 million principal amount of indebtedness and $51,000 of accrued and unpaid interest outstanding under the May 2010 Loan Facility. We may incur additional indebtedness beyond this amount, including, subject to our satisfaction of specified conditions and approval by the lenders in their sole discretion, up to $6.0 million under the May 2010 Loan Facility. Our indebtedness combined with our other financial obligations and contractual commitments, including amounts due under an equipment funding agreement with LTS could have significant adverse consequences, including:

- Requiring us to dedicate a substantial portion of our cash resources to the payment of interest on, and principal of, our debt, which will reduce the amounts available to fund working capital, capital expenditures, product development efforts and other general corporate purposes;
- Increasing our vulnerability to adverse changes in general economic, industry and competitive conditions and adverse changes in government regulation;
- Limiting our flexibility in planning for, or reacting to, changes in our business and our industry; and
- Placing us at a competitive disadvantage compared to our competitors that have less debt.

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In addition, we are vulnerable to increases in the market rate of interest because amounts outstanding under the May 2010 Loan Facility bear interest at a variable rate. If the market rate of interest increases, we may have to pay additional interest on our outstanding debt, which would reduce cash available for our other business needs. Further, we are subject to fluctuations in exchange rates because amounts due under the equipment funding agreement with LTS are in Euros. If the U.S. dollar weakens against the Euro, our costs in U.S. dollars will increase, which would also reduce cash available for our other business needs.

We may need external sources of funds to repay our indebtedness as it matures. We may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under the May 2010 Loan Facility or any other borrowings. Funds from external sources may not be available on acceptable terms, if at all. In addition, a failure to comply with the covenants under the May 2010 Loan Facility or future indebtedness could result in an event of default. In the event of an acceleration of amounts due under our debt instruments as a result of an event of default or the occurrence of a mandatory prepayment event, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness or to make any accelerated payments, and the lenders could seek to enforce security interests in the collateral securing such indebtedness.

We have a limited operating history, which makes it difficult to evaluate our business and growth prospects.

We were incorporated in Delaware in January 2005. Our operations to date have been limited to organizing and staffing our company, conducting product development activities for Zelrix and performing preclinical development of our other product candidates. As a company, we have not yet demonstrated an ability to obtain marketing approval for or commercialize a product candidate. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products as a company.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Risks Related to Our Dependence on Third Parties

We use third parties to manufacture all of our product candidates, including Zelrix, and the machinery to produce the commercial supply of Zelrix must be designed, built and validated. This may increase the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could result in clinical development and commercialization of our product candidates being delayed, prevented or impaired.

We do not own or operate, and have no plans to establish, any manufacturing facilities for our product candidates. We have limited personnel with experience in drug manufacturing and we lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale.

We currently outsource all manufacturing of our preclinical and clinical product candidates to third parties, including sumatriptan and key components of Zelrix, typically without any guarantee that there will be sufficient supplies to fulfill our requirements or that we may obtain such supplies on acceptable terms. Any delays in obtaining adequate supplies with respect to our preclinical and clinical product candidates may delay the development or commercialization of Zelrix or our other product candidates.

In addition, we do not currently have any agreements with third party manufacturers for the long-term commercial supply of our product candidates. We may be unable to enter agreements for commercial supply with third party manufacturers, or may be unable to do so on acceptable terms. Even if we enter into these agreements, the various manufacturers of each product candidate will likely be single source suppliers to us for a significant period of time.

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In particular, LTS manufactures Zelrix using sumatriptan and components that we purchase from third parties. Although LTS has considerable experience in the manufacturer of passive transdermal drug patches, it does not have experience in manufacturing active transdermal patches such as Zelrix. In order for LTS to produce our commercial supply of Zelrix, LTS must successfully complete the following:

- Transfer technology and production capabilities from its German facility where our clinical supply has been produced to its manufacturing facility in New Jersey;
- Assemble the commercial scale manufacturing equipment for Zelrix using components purchased from third party suppliers; and
- Test and validate the newly-assembled machinery and production process.

The machinery that LTS will use to produce the commercial supply of Zelrix is being customized to the particular manufacturing specifications of Zelrix and is not completed. In June 2010, we entered into an equipment funding agreement with LTS, under which we agreed to fund the purchase by LTS of the manufacturing equipment for Zelrix. If LTS is unable to assemble and validate this equipment, or to validate the production process at its New Jersey facility, in each case in a timely manner, our ability to launch and commercialize Zelrix will be compromised significantly. If this customized equipment malfunctions at any time during the production process, the time it may take LTS to secure replacement parts, to undertake repairs and to revalidate the equipment and process could limit our ability to meet the commercial demand for Zelrix.

Reliance on third party manufacturers subjects us to risks that would not affect us if we manufactured the product candidates ourselves, including:

- Reliance on the third parties for regulatory compliance and quality assurance;
- The possible breach of the manufacturing agreements by the third parties because of factors beyond our control;
- The possibility of termination or nonrenewal of the agreements by the third parties because of our breach of the manufacturing agreement or based on their own business priorities; and
- The disruption and costs associated with changing suppliers.

Our product candidates may compete with other products and product candidates for access to manufacturing facilities. There are a limited number of manufacturers that operate under current good manufacturing practice (cGMP) regulations and that are both capable of manufacturing for us and willing to do so. If our existing third party manufacturers, or the third parties that we engage in the future to manufacture a product for commercial sale or for our clinical trials, should cease to continue to do so for any reason, we likely would experience delays in obtaining sufficient quantities of our product candidates for us to meet commercial demand or to advance our clinical trials while we identify and qualify replacement suppliers. If for any reason we are unable to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively.

Our suppliers are subject to regulatory requirements, covering manufacturing, testing, quality control, manufacturing, and record keeping relating to our product candidates, and subject to ongoing inspections by the regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in long delays and interruptions to our manufacturing capacity while we seek to secure another supplier that meets all regulatory requirements.

We may rely on third parties to conduct aspects of our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be delayed in obtaining or ultimately not be able to obtain marketing approval for our product candidates.

We currently rely on contract research organizations (CROs) for some aspects of our clinical trials, including data management, statistical analysis and electronic compilation of our NDA. We may enter into additional agreements with CROs to obtain additional resources and expertise in an attempt to accelerate our progress with regard to ongoing clinical and preclinical programs. Entering into relationships with CROs involves substantial cost and requires extensive management time and focus. In addition, typically there is a transition period when a CRO commences

work. As a result, delays may occur, which may materially impact our ability to meet our desired clinical development timelines and ultimately have a material adverse impact on our operating results, financial condition or future prospects.

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As CROs are not our employees, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and preclinical programs in which they are engaged to perform. If the CROs we engage do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the data they provide is compromised due to the failure to adhere to regulatory requirements or for other reasons, then our development programs may be extended, delayed or terminated, or we may not be able to obtain marketing approval for or successfully commercialize Zelrix or any other product candidates that we develop. As a result, our financial results and the commercial prospects for Zelrix and any other product candidates that we develop would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our product candidates.

We may seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of our product candidates in the future. We may enter into such arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering into selective collaboration arrangements with leading pharmaceutical or biotechnology companies for each product candidate, both in the U.S. and internationally. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time consuming to negotiate, document and implement. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we so chose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations.

Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision making authority.

Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

Risks Related to Regulatory Matters

If we are unable to obtain marketing approval for Zelrix or our other product candidates, we will not be able to commercialize our product candidates and our business will be substantially harmed.

Our product candidates and the activities associated with their development and commercialization, including their testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the U.S. and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. As a company, we have not received approval from the FDA or demonstrated our ability to obtain marketing approval for any drugs that we have developed or are developing. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each therapeutic indication to establish the product candidate s safety and efficacy. Securing FDA approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA. Our other product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

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The process of obtaining marketing approvals is expensive and often takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved and the nature of the disease or condition to be treated. We intend to seek approval of Zelrix and likely other product candidates pursuant to Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) in the U.S., which enables an NDA applicant to rely in part on findings of safety and efficacy of a product already approved by the FDA. We may fail to obtain marketing approval for Zelrix or any other product candidates for many reasons, including the following:

- We may not be able to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for any indication;
- The results of clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for approval;
- The FDA or comparable foreign regulatory authorities may disagree with the number, design, conduct or implementation of our clinical trials;
- We may not be able to demonstrate that a product candidate s clinical and other benefits outweigh its safety risks;
- We may not be able to demonstrate that a product candidate provides an advantage over current standard of care or future competitive therapies in development;
- The FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- The FDA or comparable foreign regulatory authorities may not accept data generated at our clinical trial sites;
- The data collected from clinical trials of any product candidates that we develop may not be sufficient to support the submission of an NDA or other submission or to obtain marketing approval in the U.S. or elsewhere;
- The FDA may determine that we have identified the wrong reference listed drug or drugs or that approval of our 505(b)(2) application for Zelrix or any other product candidate is blocked by patent or non-patent exclusivity of the reference listed drug or drugs; and
- The FDA or comparable foreign regulatory authorities may identify deficiencies in the manufacturing or testing processes or facilities of third party manufacturers with which we enter into agreements for clinical and commercial supplies.

This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain marketing approval to market Zelrix or any future product candidates, which would significantly harm our business, results of operations and prospects.

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Even if we obtain marketing approval for Zelrix or any of our other product candidates, we will continue to face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if marketing approval in the U.S. is obtained, the FDA may still impose significant restrictions on a product s indicated uses or marketing, including risk evaluation and mitigation strategies, or impose ongoing requirements, including with respect to:

- Post-market surveillance, post-market studies or post-market clinical trials;
- Labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and reporting of safety and other post-market information;
- Monitoring and reporting adverse events and instances of the failure of a product to meet the specifications in the NDA;
- Changes to the approved product, product labeling or manufacturing process;
- Advertising and other promotional material; and
- Disclosure of clinical trial results on publicly available databases.

In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. The distribution, sale and marketing of our products are subject to a number of additional requirements, including:

- State wholesale drug distribution laws and the distribution of our product samples to physicians must comply with the requirements of the Prescription Drug Marketing Act;
- Sales, marketing and scientific or educational grant programs must comply with the anti-kickback and fraud and abuse provisions of the Social Security Act, the transparency provision of the Patient Protection and Affordable Care Act and an associated reconciliation bill that became law in March 2010, which we refer to collectively as the Health Care Reform Law, the False Claims Act and similar state laws;
- Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veteran s Health Care Act of 1992; and
- If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply.

All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws. If we or any third parties involved in our commercialization efforts fail to comply with applicable regulatory requirements, a regulatory agency may:

- Issue warning letters or untitled letters asserting that we are in violation of the law;
- Seek an injunction or impose civil or criminal penalties or monetary fines;
- Suspend or withdraw marketing approval;
- Suspend any ongoing clinical trials;
- Refuse to approve pending applications or supplements to applications submitted by us;
- Suspend or impose restrictions on operations, including costly new manufacturing requirements;
- Seize or detain products, refuse to permit the import or export of products, or require us to initiate a product recall;
- Refuse to allow us to enter into supply contracts, including government contracts;
- Impose civil monetary penalties; or
- Pursue civil or criminal prosecutions and fines against our company or responsible officers.

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Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenues.

Even if we obtain marketing approval for Zelrix or any of our other product candidates, adverse effects discovered after approval could limit the commercial profile of any approved product.

If we obtain marketing approval for Zelrix or any other product candidate that we develop, we or others may later discover, after use in a larger number of subjects for longer periods of time than in clinical trials, that our products could have adverse effect profiles that limit their usefulness or require their withdrawal. This discovery could have a number of potentially significant negative consequences, including:

- Regulatory authorities may withdraw their approval of the product;
- Regulatory authorities may require the addition of labeling statements, such as black box or other warnings or contraindications;
- Regulatory authorities may require us to issue specific communications to healthcare professionals, such as Dear Doctor Letters;
- Regulatory authorities may impose additional restrictions on marketing and distribution of the products;
- Regulatory authorities may issue negative publicity regarding the product, including safety communications;
- We may be required to change the way the product is administered, conduct additional clinical studies or restrict the distribution of the product;
- We could be sued and held liable for harm caused to subjects; and
- Our reputation may suffer.

Any of these events could prevent us from maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates.

We will need FDA approval of our proposed trade name, Zelrix, and any failure or delay associated with such approval may delay the commercialization of Zelrix.

Any trade name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office (USPTO). The FDA typically conducts a rigorous review of proposed trade names, including an evaluation of potential for confusion with other trade names and medical error. The FDA may also object to a trade name if it believes the name inappropriately implies medical claims. If the FDA objects to our proposed trade name, Zelrix, we may be required to adopt an alternative name for our product candidate. Even after approval, the FDA may request that we adopt an alternative name for the product if adverse event reports indicate a potential for confusion with other trade names and medical error. If we are required to adopt an alternative name, the commercialization of Zelrix could be delayed or interrupted, which would limit our ability to commercialize Zelrix and generate revenues.

If the FDA does not approve the manufacturing facilities of LTS or any future third party manufacturers for commercial production, we may not be able to commercialize Zelrix or any of our other product candidates.

The facilities used by LTS and any of our future manufacturers to manufacture Zelrix must be approved by the FDA before approval of Zelrix. We do not control the manufacturing process of Zelrix and are completely dependent on third party manufacturers for compliance with the FDA s requirements for manufacture of Zelrix. If our manufacturers cannot successfully manufacture material components and finished products that conform to our specifications and the FDA s strict regulatory requirements, they will not be able to secure FDA approval for their manufacturing facilities. If the FDA does not approve these facilities for the commercial manufacture of Zelrix, or the facilities of any of our other product candidates, we may need to find alternative manufacturing facilities, which would result in significant delays of up to several years in obtaining FDA approval for Zelrix, or any of our other product candidates. We would incur substantial additional costs as a result of any such delays, including with respect to finding alternative manufacturing facilities.

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Even if our product candidates receive marketing approval in the U.S., we may never receive marketing approval or commercialize our products outside the U.S.

In order to market Zelrix or any other product candidate outside the U.S., we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. The marketing approval process in other countries may include all of the risks associated with obtaining FDA approval in the U.S., as well as other risks. For example, legislation analogous to Section 505(b)(2) of the FDCA in the U.S., which relates to the ability of an NDA applicant to use published data not developed by such applicant, does not exist in other countries. In territories where data is not freely available, we may not have the ability to commercialize our products without negotiating rights from third parties to refer to their clinical data in our regulatory applications, which could require the expenditure of significant additional funds. Further, we may be unable to obtain rights to the necessary clinical data and may be required to develop our own proprietary safety and effectiveness dossiers. In addition, in many countries outside the U.S., it is required that a product receives pricing and reimbursement approval before the product can be commercialized. This can result in substantial delays in such countries.

Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. In addition, we may be subject to fines, suspension or withdrawal of marketing approvals, product recalls, seizure of products, operating restrictions and criminal prosecution if we fail to comply with applicable foreign regulatory requirements. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Our relationships with customers and payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with third party payors and customers will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- The federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid;
- The federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government;

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The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

The federal transparency requirements under the Health Care Reform Law requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and

Analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations could be costly. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities conducted by our sales team in the sale of Zelrix, are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell our products for which we obtain marketing approval.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Medicare Modernization Act) changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

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More recently, in March 2010, President Obama signed into law the Health Care Reform Law, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Health Care Reform Law revises the definition of average manufacturer price for reporting purposes, which could increase the amount of Medicaid drug rebates to states once the provision is effective. Further, beginning in 2011, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may require us to modify our business practices with healthcare practitioners. We will not know the full effects of the Health Care Reform Law until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the effect of the Health Care Reform Law, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Risks Related to Intellectual Property

We may not be able to rely on our intellectual property to protect our products in the marketplace.

Our success depends, in large part, on our ability to protect our competitive position through patents, trade secrets, trademarks and other intellectual property rights. The patent positions of pharmaceutical and biotechnology companies, including our company, are uncertain and involve complex questions of law and fact for which important legal issues remain unresolved or may change. As a result of recent court decisions, the requirements for patentability of inventions in the U.S. have become more stringent, including stricter requirements that inventions be non-obvious and that patent applications provide an adequate written description of the invention. These court decisions may have the effect of narrowing the types of medical treatments that are patentable.

The patent we have licensed and patents that may be licensed by or issued to us in the future may not provide us with any competitive advantage. Our patents may be challenged by third parties in patent litigation, or in patent reexamination or opposition proceedings, which are becoming widespread in the pharmaceutical industry. In particular, it is not uncommon for potential competitors to challenge the validity of patents protecting new pharmaceutical products shortly after the products receive FDA approval. Alternatively, it is possible that third parties with products that are very similar to ours will circumvent our issued patents by purposely developing products or processes that avoid our patent claims. Our patent protection may be limited because of any of the following:

- Our patents may not be broad or strong enough to prevent competition from identical or similar products;
- We may be required to disclaim part of the term of some patents;
- There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim;
- There may be prior art of which we are aware, which we do not believe affects the validity or enforceability of a claim, but which, nonetheless ultimately may be found to affect the validity or enforceability of a claim;
- If challenged, a court could determine that our issued patents are not valid or enforceable;
- A court could determine that a competitor s technology or product does not infringe our patents; and
- Our patents and patent applications could irretrievably lapse due to failure to pay fees or otherwise comply with regulations, or could be subject to compulsory licensing.

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We do not currently own any issued U.S. or foreign patents covering any of our product candidates or technology. We have licensed one issued U.S. patent that relates to an iontophoresis drug delivery system. We and our licensors have filed and are actively pursuing applications for patents in the U.S. and in foreign jurisdictions. However, pending patent applications may not result in the issuance of patents or the scope of patent protection that we have requested, and we may not develop additional proprietary products which are patentable. Further, if we encounter delays in our development or clinical trials, the period of time during which we could market our products under patent protection would be reduced.

Because the composition of matter patent covering the active pharmaceutical ingredient of Zelrix has expired, competitors will be able to offer and sell products with the same active pharmaceutical ingredient as Zelrix so long as these competitors do not infringe any other patents that may be issued to or licensed by us, including any product, formulation and method of use patents, or violate any marketing exclusivity period that may be granted. Similarly, the composition of matter patents covering the active ingredients of our NP201 and NP202 product candidates have expired, and competitors will be able to offer and sell products with the same active pharmaceutical ingredients as these product candidates products so long as these competitors do not infringe any other patents that we hold or may obtain in the future, including any product, formulation and method of use patents, or violate any marketing exclusivity period that may be granted.

Patents covering new products or formulations incorporating a generic active pharmaceutical ingredient cannot prevent competitors from commercializing the original products and formulations. In addition, method-of-use patents, in particular, are more difficult to enforce than composition of matter patents because of the risk of off label sale or use of the subject compounds. Physicians are permitted to prescribe an approved product for uses that are not described in the product s labeling. Although off label prescriptions may infringe our method of use patents, if issued, the practice is common across medical specialties and such infringement is difficult to prevent or prosecute. Off label sales would limit our ability to generate revenue from the sale of our product candidates, if approved for commercial sale. In addition, if a third party were able to design around any issued product, method, formulation or other patent and create a different product not covered by our patents, if issued, we would likely be unable to prevent that third party from manufacturing and marketing its product.

We rely on third parties to protect the intellectual property we license, including trade secrets, patents, and know-how, and we may not have any input or control over the filing, prosecution or enforcement of such intellectual property rights. Any resulting patents may be invalid or unenforceable. Any enforcement of intellectual property rights, or defense of any claims asserting the invalidity thereof, may be subject to the cooperation of the third parties.

If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to a number of license agreements and may enter into additional licenses in the future. If we fail to comply with the obligations under a license agreement or otherwise breach the license agreement, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by any previously licensed patents.

For example, we are party to a license agreement with the University of Pennsylvania (Penn), pursuant to which we license from Penn patent applications and other intellectual property related to the LAD technology to develop and commercialize licensed products, including NP201 and NP202, and a license agreement with SurModics Pharmaceuticals, Inc. (SurModics), pursuant to which we license from SurModics intellectual property to make, have made, use, sell, import and export NP201. We are obligated to pay milestone and royalty payments under each agreement in addition to other obligations. The triggering of milestone payments to Penn or SurModics depends on factors relating to the clinical and regulatory development and commercialization of NP201 and NP202, many of which are beyond our control. We may become obligated to make a milestone payment when we do not have the cash on hand to make such payment, which could require us to delay our clinical trials, curtail our operations, scale back our commercialization and marketing efforts or seek additional capital to meet these obligations on terms unfavorable to us.

Our failure to comply with the requirements of these license agreements, including our milestone payment obligations, could result in the termination of such agreements, in which case we might not be able to develop or market any product that is covered by the license. Even if we contest any such termination and are ultimately successful, our

results of operations and stock price could suffer.

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Our ability to pursue the development and commercialization of Zelrix is significantly dependent upon obtaining a license of LTS s intellectual property.

Our development and license agreement with LTS provides that if we enter into a commercial manufacturing agreement with LTS, LTS will have the exclusive right to manufacture Zelrix and LTS will grant us an exclusive, worldwide, royalty-free license under LTS s intellectual property to use, import, sell, market and distribute Zelrix. We may not enter into a commercial manufacturing agreement with LTS on commercially reasonable terms, if at all. If we do not enter into a commercial manufacturing agreement with LTS, we may not have access to LTS s proprietary technology and know-how to manufacturer Zelrix. In this situation, we would need to develop equivalent or alternative intellectual property, which will significantly delay our commercialization of Zelrix and entail significant additional cost.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our products.

Our commercial success depends significantly on our ability to operate without infringing the patents and other intellectual property rights of third parties. There could be issued patents of which we are not aware that our products infringe. There also could be patents that we believe we do not infringe, but that we may ultimately be found to infringe. Moreover, patent applications are in some cases maintained in secrecy until patents are issued. The publication of discoveries in the scientific or patent literature frequently occurs substantially later than the date on which the underlying discoveries were made and patent applications were filed. Because patents can take many years to issue, there may be currently pending applications of which we are unaware that may later result in issued patents that our products infringe. For example, pending applications may exist that provide support or can be amended to provide support for a claim that results in an issued patent that our product infringes.

Third parties may assert that we are employing their proprietary technology without authorization. If a court held that any third party patents cover our products, the holders of any such patents may be able to block our ability to commercialize our products unless we obtained a license under the applicable patent or patents, or until such patents expire. We may not be able to enter into licensing arrangements or make other arrangements at a reasonable cost or on reasonable terms. Any inability to secure licenses or alternative technology could result in delays in the introduction of our products or lead to prohibition of the manufacture or sale of products by us.

If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be significantly diminished.

In addition to patents, we rely on trade secrets and proprietary know-how to protect our intellectual property. We generally require our employees, consultants, outside scientific collaborators and sponsored researchers and other advisors to enter into confidentiality agreements. These agreements provide that all confidential information developed or made known to the individual during the course of the individual s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of our employees, the agreements also typically provide that all inventions resulting from work performed for us, utilizing our property or relating to our business and conceived or completed during employment are our exclusive property to the extent permitted by law. Where appropriate, agreements we obtain with our consultants also typically contain similar assignment of invention provisions.

These agreements may not provide meaningful protection or adequate remedies in the event of unauthorized use or disclosure of our proprietary information. Involuntary disclosure or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position. In addition, it is possible that third parties could independently develop proprietary information and techniques substantially similar to ours or otherwise gain access to our trade secrets.

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Risks Related to Employee Matters and Managing Growth

If we are not successful in attracting and retaining highly qualified personnel, including our current senior executive team, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive pharmaceutical and biotechnology industries depends in large part upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Competition for skilled personnel in our market is very intense because of the numerous pharmaceutical and biotechnology companies that seek similar personnel. These companies may have greater financial and other resources, offer a greater opportunity for career advancement and have a longer history in the industry than we do. We also experience competition for the hiring of our scientific and clinical personnel from universities and research institutions.

We are highly dependent on Jane H. Hollingsworth, our Chief Executive Officer, and Terri B. Sebree, our President. Despite our efforts to retain valuable employees, members of our management, scientific and medical teams may terminate their employment with us on short notice. We have formal employment agreements with Ms. Hollingsworth and Ms. Sebree, as well as all of our other executive officers, that each includes reasonable notice periods for terminations of such individual s employment. Besides these agreements, all other employees employment is at-will, which means that any of these employees could leave our employment at any time. We maintain key person insurance for each of Ms. Hollingsworth and Ms. Sebree. The total death benefit under each policy is $2.0 million and we are the only named beneficiary and owner of the policies. The policies have an initial term of ten years and are subject to renewal annually thereafter. We do not maintain key person insurance for any of our other employees. The loss of the services of any of our executive officers or other key employees could potentially harm our business, operating results or financial condition.

We will need to grow our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2010, we employed 26 full-time employees. We expect to expand our employee base for managerial, operational, sales, marketing, financial and other resources. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the anticipated commercialization of Zelrix or development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate or increase our revenues could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize Zelrix and our other product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Risks Related to Ownership of Our Common Stock

The market price of our common stock has been, and may continue to be, highly volatile.

The trading price of our common stock is likely to continue to be highly volatile and could be subject to wide fluctuations in price in response to various factors, many of which are beyond our control, including the following:

- Any adverse development or perceived adverse development with respect to the FDA s review of our NDA for Zelrix, including the FDA s refusal to accept the NDA for substantive review or a request for additional information;
- The commercial success of Zelrix, if approved by the FDA;
- Results of clinical trials of our product candidates or those of our competitors;

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Changes or developments in laws or regulations applicable to our product candidates;

Introduction of competitive products or technologies;

Failure to meet or exceed financial projections we provide to the public;

Actual or anticipated variations in quarterly operating results;

Failure to meet or exceed the estimates and projections of the investment community;

The perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;

General economic and market conditions and overall fluctuations in U.S. equity markets;

Developments concerning our sources of manufacturing supply;

Disputes or other developments relating to patents or other proprietary rights;

Additions or departures of key scientific or management personnel;

Issuances of debt, equity or convertible securities;

Changes in the market valuations of similar companies; and

The other factors described in this Risk Factors section.

In addition, the stock market in general, and the market for small pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management s attention and resources, which could materially and adversely affect our business and financial condition.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

To our knowledge, as of December 31, 2010, our executive officers, directors and 5% stockholders and their affiliates owned approximately 74% of our outstanding voting stock, including shares subject to outstanding options and warrants that were exercisable within 60 days after December 31, 2010. As a result, these stockholders will have significant influence and may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This concentration of ownership could delay or prevent any acquisition of our company on terms that other stockholders may desire.

Future sales of shares of our common stock, including shares issued upon the exercise of currently outstanding options and warrants could negatively affect our stock price.

A substantial portion of our outstanding common stock can be traded without restriction at any time. Some of these shares are currently restricted as a result of securities laws, but will be able to be sold, subject to any applicable volume limitations under federal securities laws with respect to affiliate sales, in the near future. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell such shares, could reduce the market price of our common stock. In addition, we have 1,415,106 shares that are subject to outstanding options and

140,520 shares that are subject to outstanding warrants. The exercise of these options and warrants and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

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Because we do not intend to pay dividends on our common stock, your returns will be limited to any increase in the value of our stock.

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business and do not anticipate declaring or paying any cash dividends on our common stock for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and our bylaws, as well as provisions of the Delaware General Corporation Law (DGCL) could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions include:

- the ability of our Board of Directors to authorize the issuance of blank check preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- the prohibition of stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- the inability of stockholders to call a special meeting of stockholders; and
- advance notice requirements for nominations for election to the board of directors and for proposing matters that can be acted upon at stockholder meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the DGCL, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders.

Our business could be negatively affected as a result of the actions of activist stockholders.

Proxy contests have been waged against many companies in the pharmaceutical industry over the last few years. If faced with a proxy contest, we may not be able to successfully respond to the contest, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest because:

- Responding to proxy contests and other actions by activist stockholders may be costly and time-consuming, and may disrupt our operations and divert the attention of management and our employees;
- Perceived uncertainties as to the potential outcome of any proxy contest may result in our inability to consummate potential acquisitions, collaborations or licensing opportunities and may make it more difficult to attract and retain qualified personnel and business partners; and
- If individuals that have a specific agenda different from that of our management or other members of our board of directors are elected to our board as a result of any proxy contest, such an election may adversely affect our ability to effectively and timely implement our strategic plan and create additional value for our stockholders.

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ITEM 1B. UNRESOLVED STAFF COMMENTS

We do not have any unresolved SEC staff comments relating to our periodic or current reports.

ITEM 2. PROPERTIES

Our corporate headquarters are located in Conshohocken, Pennsylvania, where we occupy approximately 11,075 square feet of office space and 240 square feet of storage space. The initial term of this lease ends on March 31, 2013. We also occupy approximately 480 square feet of packaging and storage space in a building adjacent to our headquarters. We occupy this storage space pursuant to a license agreement. The term of this license ends on March 31, 2013 but may be terminated earlier by the licensor for any reason upon 90 days advance written notice.

In general, these properties are adequate and suitable for the purposes for which they are being used, however, we expect to obtain additional space as we prepare for the potential commercial launch of Zelrix.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any pending legal proceedings.

ITEM 4. (REMOVED AND RESERVED)

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PART II

ITEM 5. MARKET FOR REGISTRANT S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock began trading on The NASDAQ Global Market on August 6, 2010 under the symbol PATH . Prior to that time, there was no public trading market for our common stock. The following table sets forth the high and low closing sales prices per share for our common stock for the periods indicated, as reported by The NASDAQ Global Market:

Year Ended December 31, 2010:	**High**	**Low**
Third Quarter (beginning August 6, 2010)	$ 9.61	$ 7.21
Fourth Quarter	$ 9.47	$ 5.14

Comparative Stock Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since August 6, 2010, which is the date our common stock first began trading on The NASDAQ Global Market, to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of $100 on August 6, 2010, in each of our common stock, the stocks comprising the NASDAQ Composite Index, and the stocks comprising the NASDAQ Biotechnology Index. Historical stockholder return is not necessarily indicative of the performance to be expected for any future periods.

Company/Index	**08/06/2010**	**12/31/2010**
NuPathe Inc.	$ 100.00	$ 94.28
NASDAQ Composite Index	$ 100.00	$ 118.14
NASDAQ Biotechnology Index	$ 100.00	$ 111.54

The foregoing graph and table are furnished solely with this report, and are not filed with this report, and shall not be deemed incorporated by reference into any other filing under the Securities Act or the Exchange Act, whether made by us before or after the date hereof, regardless of any general incorporation language in any such filing, except to the extent we specifically incorporate this material by reference into any such filing.

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Holders of Record

As of February 14, 2011, there were approximately 28 holders of record of our common stock. Because many of such shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Dividends

We have never paid or declared any cash dividends on our common stock. We currently intend to retain any earnings for future growth and, therefore, do not expect to pay cash dividends in the foreseeable future.

Use of Proceeds from Registered Securities

On August 11, 2010, we completed the sale of 5,000,000 shares of our common stock in our IPO at a price of $10.00 per share pursuant to a Registration Statement on Form S-1 (File No. 333-166825), which was declared effective by the SEC on August 5, 2010 (the Effective Date). After deducting underwriting discounts and commissions and other expenses of the offering, we received net offering proceeds of $43.0 million. From the Effective Date through December 31, 2010, we have used the net proceeds from the IPO as follows:

- approximately $8.0 million for further clinical development, manufacturing development, and preparation and submission of an NDA for Zelrix;
- approximately $0.9 million for the further preclinical development of NP201 and NP202; and
- approximately $2.8 million for salaries and related personnel expenses and approximately $1.4 million for working capital and other general corporate purposes.

The foregoing amounts represent the Company s reasonable estimate of the amount of net offering proceeds applied to such activities instead of the actual amount of net offering proceeds used. The remainder of the net proceeds have been invested into money market accounts. None of the net proceeds, were directly or indirectly paid to any of our directors, officers or their associates, any person(s) owning 10% or more of any class of our equity securities, or any of our affiliates, other than payments in the ordinary course of business to officers for salaries and to non-employee directors as compensation for board or board committee service.

There has been no material change in our planned use of proceeds from the IPO from that described in the final prospectus filed with the SEC pursuant to Rule 424(b) on August 6, 2010.

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ITEM 6. SELECTED FINANCIAL DATA

The selected financial data set forth below should be read in conjunction with, and is qualified by reference to, the audited financial statements and related notes contained in this Form 10-K and the information in this Form 10-K under the captions Management s Discussion and Analysis of Financial Condition and Results of Operations and Business . The statement of operations data for the years ended December 31, 2010, 2009 and 2008 and the balance sheet data as of December 31, 2010 and 2009 have been derived from our audited financial statements and related notes, which are included elsewhere in this Form 10-K. The statement of operations data for the years ended December 31, 2007 and 2006 and the balance sheet data as of December 31, 2008, 2007 and 2006 have been derived from audited financial statements which do not appear in this Form 10-K. The historical results are not necessarily indicative of the results to be expected for any future periods.

	Years Ended December 31,				
Statement of operations data:	**2010**	**2009**	**2008**	**2007**	**2006**
	(in thousands, except share and per share data)				
Revenue	$ 650	$	$	$	$
Operating expenses:					
Research and development	17,064	11,310	8,815	7,761	3,209
Acquired in-process research and development			5,500		
Selling, general and administrative	4,772	3,142	3,075	1,884	1,363
	21,836	14,452	17,390	9,645	4,572
Loss from operations	(21,186)	(14,452)	(17,390)	(9,645)	(4,572)
Interest income(expense), net	(3,670)	(1,289)	(121)	(30)	(644)
Loss before tax benefit	(24,856)	(15,741)	(17,511)	(9,675)	(5,216)
Income tax benefit	500	151			
Net loss	(24,356)	(15,590)	(17,511)	(9,675)	(5,216)
Accretion of redeemable convertible preferred stock	(2,533)	(3,617)	(2,330)	(1,126)	(341)
Net loss applicable to common stockholders	$ (26,889)	$ (19,207)	$ (19,841)	$ (10,801)	$ (5,557)
Basic and diluted net loss per common share	$ (4.39)	$ (50.31)	$ (51.98)	$ (29.38)	$ (16.25)
Weighted average basic and diluted common shares outstanding	6,126,123	381,789	381,681	367,691	341,979

	As of December 31,				
Balance sheet data:	**2010**	**2009**	**2008**	**2007**	**2006**
	(in thousands)				

Cash and cash equivalents	$ 38,918	$ 3,927	$ 8,368	$ 3,830	$ 5,211
Working capital	34,142	1,527	6,285	1,304	4,437
Total assets	43,753	5,009	9,776	4,462	5,400
Long-term debt	3,704		782	1,628	
Redeemable convertible preferred stock		55,538	41,809	16,270	10,164
Total stockholders equity (deficit)	34,265	(54,474)	(36,141)	(16,458)	(5,716)

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ITEM 7. MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis should be read together with our audited financial statements and related notes appearing elsewhere in this Form 10-K.

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of branded therapeutics for diseases of the central nervous system, including neurological and psychiatric disorders. Our most advanced product candidate, Zelrix, is an active, single-use transdermal sumatriptan patch that we are developing for the treatment of acute migraine. Zelrix uses our proprietary SmartRelief technology. We submitted a New Drug Application (NDA) for Zelrix to the U.S. Food and Drug Administration (FDA) on October 29, 2010. Subject to the approval of our NDA, we plan to build our own specialty sales force in the U.S. to launch Zelrix. We have two other proprietary product candidates in preclinical development that address large market opportunities, NP201 for the continuous symptomatic treatment of Parkinson s disease and NP202 for the long-term treatment of schizophrenia and bipolar disorder. We expect to submit an Investigational New Drug Application (IND) to the FDA in the first half of 2011 for NP201 and in 2012 for NP202.

We were incorporated in the State of Delaware in January 2005 and are a development stage company. Since our inception, we have invested a significant portion of our efforts and financial resources in the development of Zelrix. Zelrix is the only product candidate for which we have conducted clinical trials, and to date we have not marketed, distributed or sold any products. As a result, we have generated no product revenue and have never been profitable. Our net loss for the years ended December 31, 2010, 2009 and 2008 was $24.4 million, $15.6 million and $17.5 million, respectively. As of December 31, 2010, we had an accumulated deficit of $79.8 million.

We have funded our operations to date primarily with the proceeds of the sale of common stock, convertible preferred stock, preferred stock warrants, convertible notes and borrowings under credit facilities. From inception through December 31, 2010, we have received net proceeds of $101.2 million from the sale of common stock, convertible preferred stock, preferred stock warrants and convertible notes.

Liquidity and Capital Resources

We expect to continue to incur substantial additional operating losses for at least the next several years as we continue to develop our product candidates and seek marketing approval for, and the eventual commercialization of, Zelrix and our other products candidates. If we obtain marketing approval for Zelrix, we will incur significant sales, marketing and outsourced manufacturing expenses. In addition, we expect to incur additional expenses to add operational, financial and information systems and personnel to comply with corporate governance, internal controls and similar requirements applicable to us as a public company.

Our principal sources of liquidity are cash and cash equivalents of $38.9 million as of December 31, 2010. We believe that our existing cash and cash equivalents will be sufficient to fund our operations and capital requirements through FDA approval of Zelrix and into the expected commercial launch of Zelrix in the U.S. in the first half of 2012. However, changing circumstances may cause us to expend cash faster than we currently anticipate, or we may need to spend more cash than currently expected because of such circumstances. Our future capital needs and the adequacy of our available funds will depend on many factors, including:

- The outcome of the FDA s review of the NDA for Zelrix;
- The cost, scope and timing of activities undertaken to prepare for the potential commercialization of Zelrix;
- The extent to which the FDA may require us to perform additional clinical trials for Zelrix;
- The cost of purchasing manufacturing and other capital equipment for our potential products;

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The scope, progress, results and costs of development for our other product candidates;
The extent to which we acquire or invest in new products, businesses and technologies; and
The extent to which we choose to establish collaboration, co-promotion, distribution or other similar agreements for product candidates.

If additional funds are required or we elect to raise additional funds, we may raise such funds from time to time through public or private sales of equity or debt securities or from bank or other loans. Financing may not be available on acceptable terms, or at all, and our failure to raise capital when needed could materially and adversely impact our growth plans and our financial condition or results of operations. The terms of any such financing may involve significant cash payment obligations and covenants that restrict our ability to operate our business. Additionally, equity financing, if available, may be dilutive to the holders of our common stock.

We may request an additional $6.0 million in funding through May 2011 under the debt facility we entered into in May 2010 (the May 2010 Loan Facility). Any such request for additional funding would be subject to our compliance with the terms of the May 2010 Loan Facility, including the continued accuracy of our representations and warranties contained therein, and is at the lenders sole discretion. This facility has a scheduled maturity date in August 2013 and is secured by substantially all of our assets, excluding intellectual property, which is subject to a negative pledge prohibiting the granting of liens thereon to any third party.

Key Components of Our Statement of Operations

Research and Development Expenses

Our research and development expenses consist of expenses incurred in developing, testing and seeking marketing approval of our product candidates, including:

Expenses associated with regulatory submissions, preclinical development, clinical trials and manufacturing;
Personnel related expenses, such as salaries, benefits, travel and other related expenses, including stock-based compensation;
Payments made to third party investigators who perform research and development on our behalf;
Payments to third party contract research organizations, laboratories and independent contractors;
Expenses incurred to obtain technology licenses if the technology licensed has not reached technological feasibility and has no alternative future use; and
Facility, maintenance and other related expenses

We expense all research and development costs as incurred. Preclinical development expenses and clinical trial expenses for our product candidates are a significant component of our current research and development expenses. Product candidates in later stage clinical development, such as Zelrix, generally have higher research and development expenses than those in earlier stages of development, primarily due to the increased size and duration of the clinical trials. We track and record information regarding external research and development expenses for each study or trial that we conduct. From time to time, we use third party contract research organizations, laboratories and independent contractors in preclinical studies. We recognize the expenses associated with third parties performing these services for us in our preclinical studies based on the percentage of each study completed at the end of each reporting period. We coordinate clinical trials through a number of contracted investigational sites and recognize the associated expense based on a number of factors, including actual and estimated subject enrollment and visits, direct pass-through costs and other clinical site fees.

From our inception in January 2005 through December 31, 2010, we incurred research and development expenses of $54.4 million, of which $40.0 million was for the development of Zelrix (inclusive of $5.5 million of acquired in-process research and development expense in connection with the patent application utilized by Zelrix), $2.8 million was for the development of NP201 and $0.3 million was for to the development of NP202. The remaining research and development expenses are for amounts incurred that we do not allocate to specific programs, such as personnel related expenses, including salaries and benefits, as well as general fixed costs for our facility and related expenses.

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We expect that our research and development expenses in 2011 will be similar to or slightly lower than 2010 due to the fact that 2010 included substantial costs related to the completion of the full enrollment of two long-term, open label Phase III trials for Zelrix and increased regulatory expenses related to the Zelrix NDA we submitted in October. While we will continue to incur expenses related to the continued development of Zelrix, we also expect to incur research and development expenses in 2011 for the development of NP201 and NP202. These expenditures are subject to numerous uncertainties regarding timing and cost to completion. We also expect to incur additional costs relating to post-marketing studies to gather additional information regarding Zelrix s risks, benefits and optimal use.

We currently anticipate submitting an IND for NP201 in the first half of 2011 and for NP202 in 2012. Due to their early stages of development, we are not currently able to determine the duration and completion costs of our NP201 and NP202 development projects.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries, benefits and other related costs, including stock-based compensation, for personnel serving in our executive, finance, accounting, legal, market research and human resource functions. Our selling, general and administrative expenses also include facility and related costs not included in research and development expenses, professional fees for legal, including patent-related expenses, expenses related to market research and commercialization preparation activities, consulting, tax and accounting services, insurance, depreciation and general corporate expenses.

We expect that our selling, general and administrative expenses in 2011 will be significantly higher than in 2010 as a result of higher expenses in 2011 for costs related to building a commercial infrastructure for the anticipated U.S. launch of Zelrix in the first half of 2012. Additionally, we expect higher expenses relating to a full year of operating as a public company, including increased costs for the hiring of additional personnel, and for payment to outside consultants, including lawyers and accountants, to comply with additional regulations, corporate governance, internal control and similar requirements applicable to public companies, as well as increased costs for insurance.

Interest Income and Interest Expense

Interest income consists of interest earned on our cash and cash equivalents. Interest expense consists primarily of cash and non-cash interest costs related to our outstanding debt. Additionally, in connection with some of our debt financings, we issued warrants, the fair value of which we recorded as deferred financing costs. We amortize these deferred financing costs over the lives of the loans as interest expense in our statement of operations. Prior to our initial public offering (IPO), on a quarterly basis these warrants were marked-to-market, in accordance with accounting principles generally accepted in the U.S (GAAP), and any change in fair value was recorded as interest expense in our statement of operations. Upon the completion of our IPO, these warrants were reclassified into stockholders equity as they were converted into warrants to purchase common stock and are no longer required to be marked-to-market at each balance sheet date. We expect cash-paid interest expense to increase in 2011 compared with 2010 as a result of the May 2010 Loan Facility. We do not anticipate significant non-cash interest expense in 2011.

Net Operating Losses and Tax Loss Carryforwards

Our net loss was $24.4 million for the year ended December 31, 2010 and $15.6 million for the year ended December 31, 2009. We have incurred cumulative net losses of $73.4 million from inception through December 31, 2010. As of December 31, 2010, we had approximately $64.9 million of federal net operating loss carryforwards and state research and development credits available to offset future taxable income. These federal and state net operating loss carryforwards will begin to expire in 2025. Due to the uncertainty of our ability to realize the benefit of any net operating loss carryforwards and credits, the deferred tax asset related to these carryforwards has been fully offset by a valuation allowance at December 31, 2010.

Our IPO, together with private placements and other transactions that have occurred since our inception, may trigger, or may have already triggered, an ownership change pursuant to Section 382 of the Code. If an ownership change is triggered, it will limit our ability to use some of our net operating loss carryforwards. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo further ownership changes in the future, which could further limit our ability to use net operating loss carryforwards. As a result, if we generate taxable income, our ability to use some of our net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations.

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Critical Accounting Policies and Use of Estimates

This Management s Discussion and Analysis of Our Financial Condition and Results of Operations discusses our financial statements, which have been prepared in accordance with GAAP and are included in this Form 10-K. The preparation of these financial statements in accordance with GAAP requires us to make estimates that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements as well as the reported expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those related to clinical trial expenses and stock-based compensation. We base our estimates on historical experience and on various other factors that we believe to be appropriate under the circumstances. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully discussed in note 3 to our financial statements, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our financial statements. We have reviewed these critical accounting policies and estimates with the audit committee of our board of directors.

Research and Development Expenses

Although we manage the conduct of our own clinical trials, we rely on third parties to conduct our preclinical studies and to provide services, including data management, statistical analysis and electronic compilation for our clinical trials, as well as for the manufacture of our clinical trial supplies. At the end of each reporting period, we compare the payments made to each service provider to the estimated progress towards completion of the related project. Factors that we consider in preparing these estimates include the number of subjects enrolled in studies, milestones achieved and other criteria related to the efforts of our vendors. These estimates are subject to change as additional information becomes available. Depending on the timing of payments to vendors and estimated services provided, we record net prepaid or accrued expenses related to these costs. We calculate expenses incurred for the manufacture of our clinical supplies using our estimate of costs and capitalize these expenses on our balance sheet to the extent we hold clinical supply materials on hand to be distributed for use in our clinical trials. We expense these costs as the supplies are consumed in the trials.

Stock-Based Compensation

We use the Black-Scholes option-pricing model to value our stock option awards. The Black-Scholes option-pricing model requires the input of subjective assumptions, including the expected life of stock options, stock price volatility and the risk-free interest rate. The risk-free interest rate is based on U.S. Treasury instruments with a remaining term equal to the expected term of the option. As a newly public company, we do not have sufficient history to estimate the expected life of our options or the volatility of our common stock price. We use comparable public companies as a basis for our expected volatility to calculate the fair value of our option grants. We intend to continue to consistently apply this process using comparable companies until a sufficient amount of historical information regarding the volatility of our own share price becomes available. We use the simplified method, as allowed under the Securities and Exchange Commission s, or SEC, accounting guidance, to determine the expected life, which is the midpoint between an option s vesting date and contractual term. The assumptions used in calculating the fair value of stock options represent our best estimate and involve inherent uncertainties and the application of our judgment. As a result, if factors change and we use different assumptions, stock-based compensation could be materially different in the future.

Prior to our IPO, the fair value of our common stock underlying grants of common stock options and restricted stock was determined by our board of directors, or compensation committee pursuant to authority delegated by our board of directors, and represented the most important factor in determining the value of our stock-based compensation. In the absence of a public trading market for our common stock, our board of directors or compensation committee was required to estimate the fair value of our common stock at the grant date of our stock-based awards. In estimating our aggregate equity value, we used methodologies and assumptions consistent with the American Institute of Certified Public Accountants Practice Guide, or the AICPA Practice Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. The primary methodologies that we considered to determine our aggregate equity value were a market-based approach and an asset-based approach.

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Impact of Recent Accounting Pronouncements

In January 2010, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2010-06, Fair Value Measurements and Disclosures (Topic 820): Improving Disclosures about Fair Value Measurements (ASU 2010-06), which amends the existing fair value measurement and disclosure guidance currently included in Accounting Standards Codification (ASC) Topic 820, Fair Value Measurements and Disclosures, to require additional disclosures regarding fair value measurements. Specifically, ASU 2010-06 requires entities to disclose the amounts of significant transfers between Level 1 and Level 2 of the fair value hierarchy and the reasons for these transfers, the reasons for any transfer in or out of Level 3 and information in the reconciliation of recurring Level 3 measurements about purchases, sales, issuances and settlements on a gross basis. In addition, ASU 2010-06 also clarifies the requirement for entities to disclose information about both the valuation techniques and inputs used in estimating Level 2 and Level 3 fair value measurements. ASU 2010-06 is effective for interim and annual reporting periods beginning after December 15, 2009, except for additional disclosures related to Level 3 fair value measurements, which are effective for fiscal years beginning after December 15, 2010. The adoption of ASU 2010-06 did not impact the Company s financial statements.

Results of Operations

Comparison of Years Ended December 31, 2010 and 2009

Revenue

During the year ended December 31, 2010, the Company was awarded $650,000 of Qualifying Therapeutic Discovery Project (QTDP) grants under section 48D of the U.S. Internal Revenue Code in connection with costs incurred during 2009 and 2010 for the Company s Zelrix, NP201 and NP202 development programs. Under the award guidelines, QTDP s had to show a reasonable potential to result in new therapies to treat areas of unmet medical need or prevent, detect or treat chronic or acute diseases and conditions, reduce the long-term growth of health care costs in the United States, or significantly advance the goal of curing cancer within 30 years.

Research and Development Expenses

Research and development expenses for the years ended December 31, 2010 and 2009 were comprised of the following:

	Year Ended December 31,		Increase (Decrease)	
	2010	2009	$	%
	(In thousands)			
Clinical development	$ 5,813	$ 4,411	$ 1,402	32%
Manufacturing	4,965	2,490	2,475	99
Preclinical development		1,268	(1,268)	(100)
Regulatory and quality assurance	2,571	179	2,392	1,336
Compensation and related	3,019	2,388	631	26
Facilities and related	696	574	122	21
	$ 17,064	$ 11,310	$ 5,754	51

Research and development expenses increased by $5.8 million, or 51%, to $17.1 million in 2010 from $11.3 million in 2009. This increase resulted primarily from a $2.5 million increase in manufacturing costs related to production of Phase III clinical supplies of Zelrix, a $2.4 million increase in regulatory and quality assurance costs related to the preparation and filing of our Zelrix NDA in October 2010, and a $1.4 million increase in clinical development costs due to our continued Phase III clinical program for Zelrix. These increases were, in part, offset by a $1.3 million decrease in preclinical expenses, reflecting the completion in 2009 of a substantial portion of our preclinical studies for Zelrix and our increased focus on our Phase III clinical program for Zelrix in 2010. Research and development headcount remained fairly flat for 2010 as compared to 2009, with the increase in compensation and related expenses resulting from annual increases in salary, bonus, stock-based compensation expense and benefit premiums.

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Research and development expenses by program for the years ended December 31, 2010 and 2009 are presented below:

	Year Ended December 31,		Increase (Decrease)	
	2010	2009	$	%
	(In thousands)			
Zelrix	$ 12,225	$ 8,183	$ 4,042	49%
NP201	1,096	244	852	349
NP202	274		274	100
General development	3,469	2,883	586	20
	$ 17,064	$ 11,310	$ 5,754	51

The increase in spending on Zelrix in 2010 was primarily due to the continuation of our Phase III clinical programs and the related manufacture of Phase III clinical supplies, as well as the preparation of our Zelrix NDA which was submitted in October 2010. These expenses were partially offset by lower preclinical spending due to the completion of many of our preclinical studies in 2009. Increased spending on NP201 in 2010, compared to 2009, was primarily the result of additional formulation (manufacturing) work. Modest spending on NP202 began in the second half of 2010 as we began early research and development. Personnel related expenses, including salaries and benefits, are included in the table above as general development expenses as we do not allocate these expenses to specific programs.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased by $1.6 million, or 52%, to $4.8 million in 2010 from $3.1 million in 2009. This increase resulted primarily from higher personnel costs due to additional employees as well as salary increases, higher stock-based compensation expense and expenses related to being a public company, such as increased public accounting expense and board of director s fees.

Interest Expense

Interest expense increased by $2.4 million to $3.7 million in 2010 from $1.3 million in 2009. The 2010 expense is comprised of $2.6 million of non-cash interest expense incurred during 2010 that was related to the amortization of the beneficial conversion feature (BCF) of secured subordinated promissory notes that we issued and sold to investors in April 2010 (April 2010 Convertible Notes), plus an additional $0.3 million of non-cash interest accrued on these notes prior to their conversion, and an additional $0.3 million of non-cash interest expense for the increase in fair value of our warrant liability that occurred during 2010 before the warrants were reclassified to stockholders equity upon the completion of our IPO. Also included in the 2010 interest expense is $0.2 million of non-cash amortization of deferred debt issuance costs and $0.4 million of cash-paid interest on our outstanding debt. During 2009, the Company had $1.1 million of non-cash interest expense related to the issuance and subsequent conversion of the convertible promissory notes issued in July 2009 and $0.2 million of cash-paid interest on our outstanding debt.

Income Tax Benefit

We recognized an income tax benefit of $0.5 million in 2010 and $0.2 million in 2009 related to the sale of Pennsylvania research and development tax credits to third party buyers.

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Comparison of Years Ended December 31, 2009 and 2008

Research and Development Expenses

Research and development expenses for the years ended December 31, 2009 and 2008 were comprised of the following:

	Year Ended December 31,		Increase (Decrease)	
	2009	2008	$	%
	(In thousands)			
Clinical development	$ 4,411	$ 1,195	$ 3,216	269%
Manufacturing	2,490	3,051	(561)	(18)
Preclinical development	1,268	1,912	(644)	(34)
Regulatory and quality assurance	179	224	(45)	(20)
Compensation and related	2,388	1,950	438	22
Facilities and related	574	483	91	19
	$ 11,310	$ 8,815	$ 2,495	28

Research and development expenses increased by $2.5 million, or 28%, to $11.3 million in 2009 from $8.8 million in 2008. This increase resulted primarily from a $3.2 million increase in clinical development costs related to our pivotal Phase III clinical trial and our long term, open label Phase III trials for Zelrix and a $0.4 million increase in compensation and related costs, offset by a $0.6 million decrease in preclinical expenses and a $0.6 million decrease in manufacturing expenses. The increase in compensation and related costs in 2009 primarily reflected our addition of research and development personnel, particularly in the areas of quality assurance, regulatory and medical, throughout 2008. The costs of these additional personnel were reflected as a full year of expense in 2009. The decrease in preclinical expense in 2009 primarily reflected the completion of a preclinical NP201 study in the first half of 2009, which had been ongoing throughout 2008. The decrease in manufacturing expenses in 2009 primarily reflected prototype development work in 2008 for NP201 that did not recur in 2009.

Research and development expenses by program for the years ended December 31, 2009 and 2008 are presented below:

	Year Ended December 31,		Increase (Decrease)	
	2009	2008	$	%
	(In thousands)			
Zelrix	$ 8,183	$ 5,590	$ 2,593	46%
NP201	244	743	(499)	(67)
General development	2,883	2,482	401	16
	$ 11,310	$ 8,815	$ 2,495	28

The significant increase in spending on Zelrix in 2009 was primarily due to the continuation of our Phase III clinical program. As we completed and analyzed the results of our preclinical trial for NP201, our spending on NP201 declined by 67% in 2009. Personnel related expenses, including salaries and benefits, are included in the table above as general development expenses as we do not allocate these costs to specific product candidates.

Acquired In-Process Research and Development Expenses

In July 2008, we entered into an asset purchase and license agreement with Travanti Pharma Inc., or Travanti. Pursuant to the terms of the Travanti agreement, we paid $5.5 million to Travanti for the purchase of a patent application, and a worldwide license in the field of migraine to additional intellectual property, related to transdermal

delivery of anti-migraine medications using an active delivery patch. We recognized the purchase price in our statement of operations for the year ended December 31, 2008 as acquired in-process research and development because additional research and development efforts and marketing approval in the U.S. is required in order to commercialize Zelrix, which utilizes this patent application.

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Selling, General and Administrative Expenses

Selling, general and administrative expenses were $3.1 million in both 2009 and 2008. Although selling, general and administrative compensation expenses increased by $0.4 million in 2009 due, in part, to the hiring of a chief financial officer in the fourth quarter of 2008, this increase was offset by decreases of $0.2 million in legal expenses, $0.1 million in market research expenses and $0.1 million in other general expenses.

Interest Income/Expense

Interest income decreased to $30,000 in 2009 from $158,000 in 2008 due to lower average cash and cash equivalent balances, consisting primarily of bank deposits and money market mutual funds invested in short-term corporate and government obligations, and lower yields on investments.

Interest expense increased to $1.3 million in 2009 from $0.3 million in 2008 primarily as a result of the non-cash beneficial conversion feature and the fair value of the warrants issued in connection with the issuance of convertible debt in July 2009. This convertible debt converted into shares of Series B preferred stock in August 2009.

Income Tax Benefit

In 2009, we recognized an income tax benefit of $151,000 related to the sale of Pennsylvania research and development tax credits to a third party buyer.

Cash Flows

Net cash used in operating activities in 2010 was $18.4 million, primarily the result of spending on our Phase III clinical program for Zelrix and the related manufacture of supplies for those trials, as well as costs incurred for the preparation and filing of our Zelrix NDA. During the year ended December 31, 2010, we used $3.5 million of cash in investing activities, almost solely for the purchase of equipment related to the commercial manufacture of Zelrix. These payments represent the first seven of fourteen scheduled payments to be made for this equipment that total $7.1 million based on exchange rates in effect at December 31, 2010. Also in the year ended December 31, 2010, we were provided with $56.9 million from financing activities, primarily from the $43.0 million of net proceeds received from our IPO, combined with $10.1 million from the April 2010 Convertible notes and $5.0 million from the May 2010 Loan Facility. These cash inflows from financings are offset by $1.2 million of contractual debt repayments throughout 2010.

Net cash used in operating activities in 2009 was $13.6 million, primarily the result of spending on our pivotal Phase III clinical trial as well as our long-term, open label Phase III trials for Zelrix, and the related manufacture of supplies for these trials. During the year ended December 31, 2009, we used $29,000 in investing activities for the purchase of property and equipment. Cash provided by financing activities in 2009 was $9.2 million, reflecting $10.1 million of net proceeds from the sale of Series B preferred stock, partially offset by scheduled debt repayments of $0.9 million.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not have as of the filing of this 10-K with the SEC, any off-balance sheet arrangements as defined in Item 3(a)(4) of the SEC s Regulation S-K.

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Contractual Obligations

The following table summarizes our contractual obligations as of December 31, 2010:

	Payments Due by Period				
Contractual Obligations(1)	**Total**	**2011**	**2012 and 2013**	**2014 and 2015**	**2016 and Thereafter**
			(In thousands)		
Debt obligations	$ 5,217	$ 1,513	$ 3,704	$	$
Interest payments on debt	946	559	387		
License maintenance fees(2)	350	50	100	100	100
Operating lease obligations	823	363	460		
Development expenditures(3)	1,750	250	500	500	500
Equipment Funding (4)	3,595	3,595			
	$ 12,681	$ 6,330	$ 5,151	$ 600	$ 600

(1) This table does not include any contingent milestone or royalty payments that may become payable to third parties under license agreements because the timing and likelihood of such payments are not known.

(2) Under an agreement with the University of Pennsylvania (Penn), we are required to pay annual license maintenance fees of up to $50,000 until the first commercial sale of the first licensed product covered by the agreement. The agreement currently covers NP201 and NP202. Because we cannot currently estimate when the first sale of a licensed product will occur, the table reflects payments only through 2017.

(3) Under the agreement with Penn discussed in footnote 2 to this table, we are required to expend an aggregate of at least $250,000 annually toward the development and commercialization of NP201 and NP202, until the first commercial sale of the first licensed product under the agreement. Because we cannot currently estimate when the first sale of a licensed product will occur, the table reflects payments only through 2017.

(4) Under an agreement with LTS Lohmann Therapie-Systeme AG (LTS), we are required to pay to LTS an aggregate of 5.4 million in 14 monthly installments that commenced in June 2010 for the purchase of manufacturing equipment for Zelrix. As of December 31, 2010, 2.7 million, or approximately $3.6 million based on exchange rates as of December 31, 2010, remains to be paid.

In addition to the contractual commitments reflected in the table above, we have agreed to pay Penn aggregate milestone payments of up to $950,000, per licensed product, upon the achievement of specified development and regulatory milestones related to each licensed product that contains ropinirole and other specified active ingredients, including the active ingredients in NP201 and NP202, and royalties in the low single digits on worldwide net sales of such licensed products. We and Penn have agreed to negotiate the milestone payments and royalties payable for each licensed product that contains an active ingredient other than those currently specified in the agreement. We are unable to determine the timing of the achievement of these milestones or whether and when we will commercialize and generate any sales for a licensed product.

We have also entered into a license agreement with SurModics under which we have agreed to pay SurModics milestone payments of up to an aggregate amount of $4.75 million upon the achievement of specified development, regulatory and sales level milestones related to the first clinical indication approved by a regulatory authority for NP201. We must also pay an additional single milestone payment upon regulatory approval of each additional clinical indication for NP201 and royalties in the low single digits on worldwide net sales of commercial product. We are unable to determine the timing of the achievement of these milestones or whether and when we will commercialize

and generate any sales for a licensed product.

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ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The primary objective of our investment activities is to preserve our capital to fund operations. We also seek to maximize income from our investments without assuming significant risk. Our exposure to market risk is confined to our cash and cash equivalents. As of December 31, 2010, we had cash and cash equivalents of $38.9 million. We do not engage in any hedging activities against changes in interest rates. Because of the short-term maturities of our cash and cash equivalents, we do not believe that an increase in market rates would have any significant impact on the realized value of our investments, but may increase the interest expense associated with our debt.

We have no operations outside the U.S. We have, however, entered into two agreements with LTS, a manufacturer in Germany. Under one of these agreements, LTS provides services to us related to the production and assembly of Zelrix. Under this agreement, we paid $2.1 million in 2008, $1.2 million in 2009 and $1.6 million in the year ended December 31, 2010 to LTS. Under the other agreement, we have agreed to pay LTS an aggregate of 5.4 million in 14 monthly installments that commenced in June 2010, to fund the purchase of commercial manufacturing equipment for Zelrix. As of December 31, 2010, 2.7 million, or approximately $3.6 million, based on exchange rates as of December 31, 2010, remain to be paid.

Because of these agreements, we are subject to fluctuations in the exchange rate between the U.S. dollar and the Euro. We do not engage in any hedging activities against changes in the exchange rate between the U.S. dollar and the euro because we believe reasonably possibly near-term fluctuations of such exchange rate would not materially affect our results of operations, financial position or cash flows. We are currently in the process of transferring these manufacturing activities to one of LTS s U.S. subsidiaries and anticipate that our commercial manufacturing activities will be located in the U.S., thereby substantially eliminating our exposure to fluctuation in the relative values of the U.S. dollar and the Euro.

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ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO FINANCIAL STATEMENTS
NUPATHE INC.
(A Development-Stage Company)

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
NuPathe Inc.:

We have audited the accompanying balance sheets of NuPathe Inc. (a development-stage company) (the Company) as of December 31, 2010 and 2009, and the related statements of operations, redeemable convertible preferred stock and stockholders equity (deficit), and cash flows for each of the years in the three-year period ended December 31, 2010 and the period from January 7, 2005 (inception) through December 31, 2010. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of NuPathe Inc. as of December 31, 2010 and 2009, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2010 and for the period from January 7, 2005 (inception) through December 31, 2010, in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP
Philadelphia, Pennsylvania
March 18, 2011

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NUPATHE INC.
(A Development-Stage Company)
Balance Sheets

	December 31, 2010	December 31, 2009
ASSETS		
Current assets:		
Cash and cash equivalents	$ 38,918,332	$ 3,926,574
Prepaid expenses and other	1,007,774	918,878
Total current assets	39,926,106	4,845,452
Property and equipment, net	98,266	70,628
Other assets	318,218	93,053
Other assets-equipment funding (note 9(c))	3,410,315	
Total assets	$ 43,752,905	$ 5,009,133
LIABILITIES AND STOCKHOLDERS EQUITY (DEFICIT)		
Current liabilities:		
Current portion of long-term debt	$ 1,512,867	$ 818,139
Accounts payable	1,198,177	1,464,106
Accrued expenses	3,073,017	1,035,826
Total current liabilities	5,784,061	3,318,071
Long-term debt	3,703,704	
Warrant liability		626,492
Total liabilities	9,487,765	3,944,563
Commitments (note 9)		
Redeemable convertible preferred stock, $0.001 par value; authorized 10,000,000 and 71,745,055 shares at December 31, 2010 and December 31, 2009, respectively; issued and outstanding 53,096,340 shares as of December 31, 2009		55,538,191
Stockholders equity (deficit):		
Common stock, $0.001 par value; authorized 90,000,000 shares; issued and outstanding 14,549,461 and 390,676 shares at December 31, 2010 and December 31, 2009, respectively	14,549	390
Additional paid-in capital	114,046,923	
Deficit accumulated during the development stage	(79,796,332)	(54,474,011)
Total stockholders equity (deficit)	34,265,140	(54,473,621)

Total liabilities and stockholders equity (deficit)	$ 43,752,905	$ 5,009,133

See accompanying notes to financial statements.

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NUPATHE INC.
(A Development-Stage Company)
Statements of Operations

	Year Ended December 31,			Period from January 7, 2005 (inception) through December 31,
	2010	2009	2008	2010
Grant revenue	$ 649,959	$	$	$ 649,959
Operating expenses:				
Research and development	17,063,840	11,309,503	8,815,354	48,851,409
Acquired in-process research and development			5,500,000	5,500,000
Selling, general and administrative	4,771,645	3,142,253	3,075,084	14,599,027
	21,835,485	14,451,756	17,390,438	68,950,436
Loss from operations	(21,185,526)	(14,451,756)	(17,390,438)	(68,300,477)
Interest income	47,037	30,437	157,622	573,510
Interest expense	(3,717,686)	(1,320,005)	(278,387)	(6,340,223)
Loss before tax benefit	(24,856,175)	(15,741,324)	(17,511,203)	(74,067,190)
Income tax benefit	500,388	151,012		651,400
Net loss	(24,355,787)	(15,590,312)	(17,511,203)	$ (73,415,790)
Accretion of redeemable convertible preferred stock	(2,533,495)	(3,617,211)	(2,330,344)	
Net loss available to common stockholders	$ (26,889,282)	$ (19,207,523)	$ (19,841,547)	
Basic and diluted net loss per common share	$ (4.39)	$ (50.31)	$ (51.98)	
Weighted average basic and diluted common shares outstanding	6,126,123	381,789	381,681	

See accompanying notes to financial statements.

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NUPATHE INC.
(A Development-Stage Company)
Statements of Redeemable Convertible Preferred Stock and Stockholders Equity (Deficit)
Period from January 7, 2005 (inception) through December 31, 2010

	Redeemable Convertible Preferred Stock		Stockholders Equity (Deficit)				
			Common Stock		Additional	Deficit Accumulated	
	Shares	Amount	Shares	Amount	Paid-in Capital	During the Development Stage	Total
Balance, January 7, 2005 (inception)		$		$	$	$	$
Issuance of common stock to initial stockholders at $0.64 per share			338,116	338	216,462		216,800
Net loss						(1,067,659)	(1,067,659)
Balance, December 31, 2005			338,116	338	216,462	(1,067,659)	(850,859)
Stock-based compensation			114,158	114	43,996		44,110
Conversion of convertible notes and accrued interest into Series A redeemable convertible preferred stock	3,481,645	2,590,343			647,587		647,587
Sale of Series A redeemable convertible preferred stock at $0.93 per share, net of expenses of $267,458	8,064,516	7,232,542					
Accretion of Series A redeemable convertible preferred stock to redemption value		340,998			(340,998)		(340,998)
Net loss						(5,215,756)	(5,215,756)
	11,546,161	10,163,883	452,274	452	567,047	(6,283,415)	(5,715,916)

Balance, December 31, 2006							
Stock-based compensation					59,205		59,205
Sale of Series A redeemable convertible preferred stock at $0.93 per share, net of expenses of $20,272	5,376,345	4,979,729					
Accretion of Series A redeemable convertible preferred stock to redemption value		1,126,265			(626,252)	(500,013)	(1,126,265)
Net loss						(9,675,073)	(9,675,073)
Balance, December 31, 2007	16,922,506	16,269,877	452,274	452		(16,458,501)	(16,458,049)
Stock-based compensation					158,176		158,176
Exercise of stock options			155		225		225
Sale of Series A redeemable convertible preferred stock at $0.93 per share	2,688,171	2,499,999					
Sale of Series B redeemable convertible preferred stock at $0.93 per share, net of expenses of $304,368	22,594,385	20,708,410					
Accretion of Series A and Series B redeemable convertible preferred stock to redemption value		2,330,344			(158,401)	(2,171,943)	(2,330,344)
Net loss						(17,511,203)	(17,511,203)
Balance, December 31, 2008	42,205,062	41,808,630	452,429	452		(36,141,647)	(36,141,195)

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	Redeemable Convertible Preferred Stock		Stockholders Equity (Deficit)				
			Common Stock		Additional	Deficit Accumulated	
	Shares	Amount	Shares	Amount	Paid-in Capital	During the Development Stage	Total
Stock-based compensation		$		$	$ 319,055	$	$ 319,055
Forfeiture of restricted stock			(61,753)	(62)	62		
Sale of Series B redeemable convertible preferred stock at $0.93 per share, net of expenses of $16,538	8,786,952	8,155,327					
Conversion of convertible notes and accrued interest into Series B redeemable convertible preferred stock	2,104,326	1,957,023					
Beneficial conversion feature related to the convertible note and warrant agreement					556,042		556,042
Accretion of Series A and Series B redeemable convertible preferred stock to redemption value		3,617,211			(875,159)	(2,742,052)	(3,617,211)
Net loss						(15,590,312)	(15,590,312)
Balance, December 31, 2009	53,096,340	55,538,191	390,676	390		(54,474,011)	(54,473,621)

Stock-based compensation					543,350		543,350
Exercise of stock options			4,878	5	7,566		7,571
Accretion of Series A and Series B redeemable convertible preferred stock to redemption value		2,533,495			(1,566,961)	(966,534)	(2,533,495)
Conversion of preferred stock including accrued dividends, into common stock	(53,096,340)	(58,071,686)	7,861,785	7,862	58,063,824		58,071,686
Sale of common stock net of expenses of $7,028,009			5,000,000	5,000	42,966,991		42,971,991
Conversion of convertible notes and accrued interest into common stock			1,292,122	1,292	10,335,717		10,337,009
Beneficial conversion feature related to convertible notes and warrant agreements					2,583,617		2,583,617
Reclassification of warrants to purchase common stock					1,112,819		1,112,819
Net loss						(24,355,787)	(24,355,787)
Balance, December 31, 2010		$	14,549,461	$ 14,549	$ 114,046,923	$ (79,796,332)	$ 34,265,140

See accompanying notes to financial statements.

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NUPATHE INC.
(A Development-Stage Company)
Statements of Cash Flows

	Year Ended December 31,			Period from January 7, 2005 (inception) through December 31,
	2010	2009	2008	2010
Cash flows from operating activities:				
Net loss	$ (24,355,787)	$ (15,590,312)	$ (17,511,203)	$ (73,415,790)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation expense	46,649	57,383	48,197	177,474
Loss on asset disposal		23,508		23,508
Acquired in-process research and development			5,500,000	5,500,000
Stock-based compensation	543,350	319,055	158,176	1,132,696
Noncash interest expense	3,336,744	1,154,486	49,503	5,225,136
Changes in operating assets and liabilities:				
Prepaid expenses and other assets	299,879	301,090	(702,692)	(532,577)
Accounts payable	(265,929)	543,684	(11,149)	1,198,177
Accrued expenses	1,991,746	(376,524)	195,537	3,151,942
Net cash used in operating activities	(18,403,348)	(13,567,630)	(12,273,631)	(57,539,434)
Cash flows from investing activities:				
Purchase of in-process research and development			(5,500,000)	(5,500,000)
Payments under equipment funding agreement	(3,410,315)			(3,410,315)
Purchases of property and equipment	(74,287)	(28,792)	(126,677)	(299,247)
Net cash used in investing activities	(3,484,602)	(28,792)	(5,626,677)	(9,209,562)
Cash flows from financing activities:				
Proceeds from issuance of debt	5,000,000		100,749	7,608,741
Proceeds from convertible notes	10,062,500	1,934,183		14,466,683
Payment of debt issuance costs	(174,324)			(248,358)
Repayment of debt	(988,030)	(934,975)	(870,879)	(2,923,532)
Proceeds from sale of preferred stock, net		8,155,327	23,208,409	43,576,007
Proceeds from sale of common stock, net	42,979,562		225	43,187,787
Net cash provided by financing activities	56,879,708	9,154,535	22,438,504	105,667,328
Net increase (decrease) in cash and cash equivalents	34,991,758	(4,441,887)	4,538,196	38,918,332

Cash and cash equivalents, beginning of period	3,926,574	8,368,461	3,830,265	
Cash and cash equivalents, end of period	$ 38,918,332	$ 3,926,574	$ 8,368,461	$ 38,918,332
Supplemental cash flow disclosures:				
Noncash investing and financing activities:				
Conversion of note principal and accrued interest to redeemable convertible preferred stock	$	$ 1,957,023	$	$ 4,547,366
Conversion of note principal and accrued interest to common stock	10,337,009			10,337,009
Conversion of preferred stock plus accrued dividends to common stock	58,071,686			58,071,686
Reclassification of warrant liability	1,112,819			1,112,819
Accretion of redeemable convertible preferred stock	2,533,495	3,617,211	2,330,344	9,948,311
Cash paid for interest	380,942	173,580	236,078	983,747

See accompanying notes to financial statements.

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NUPATHE INC.
(A Development-Stage Company)
Notes to Financial Statements

(1) Background

NuPathe Inc. (the Company) is a specialty pharmaceutical company focused on the development and commercialization of branded therapeutics for diseases of the central nervous system. The Company was incorporated in Delaware on January 7, 2005 (inception) and has its principal office in Conshohocken, Pennsylvania. The Company operates as a single business segment and is a development stage company.

(2) Development-Stage Risks and Liquidity

The Company has incurred losses and negative cash flows from operations since inception and has accumulated a deficit during the development stage of $79,796,332 as of December 31, 2010. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant sales of its products currently in development. Management estimates that cash and cash equivalents of $38,918,332 as of December 31, 2010, will be sufficient to fund operations and capital requirements into the first half of 2012. Additional financing will be needed by the Company to fund its operations and the commercialization of its products beyond the first half of 2012. There is no assurance that such financing will be available when needed or on acceptable terms.

The Company is subject to those risks associated with any development-stage specialty pharmaceutical company that has substantial expenditures for research and development. There can be no assurance that the Company s research and development projects will be successful, that products developed will obtain necessary regulatory approval, or that any approved product will be commercially successful. In addition, the Company operates in an environment of rapid technological change, and is largely dependent on the services of its employees and consultants.

(3) Summary of Significant Accounting Policies

(a) Use of Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from such estimates.

(b) Fair Value of Financial Instruments

Management believes that the carrying amounts of the Company s financial instruments, including cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses, approximate fair value due to the short-term nature of those instruments. The carrying amount of the Company s debt obligations approximate fair value based on interest rates available on similar borrowings.

The Company follows Financial Accounting Standards Board (FASB) accounting guidance on fair value measurements for financial assets and liabilities measured on a recurring basis. The guidance requires fair value measurements be classified and disclosed in one of the following three categories:

Level 1: Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities;

Level 2: Quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liabilities; or

Level 3: Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

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The following fair value hierarchy table presents information about each major category of the Company s financial assets and liability measured at fair value on a recurring basis as of December 31, 2010 and 2009:

	Fair Value Measurement at Reporting Date Using			
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
At December 31, 2010				
Assets				
Cash equivalents	$ 38,770,210	$	$	$ 38,770,210
At December 31, 2009				
Assets				
Cash equivalents	$ 3,654,831	$	$	$ 3,654,831
Liabilities				
Warrant liability	$	$	$ 626,492	$ 626,492

The reconciliation of warrant liability measured at fair value on a recurring basis using unobservable inputs (Level 3) is as follows:

	Warrant Liability
Balance at January 1, 2009	$ 102,354
Issuance of additional warrants	556,042
Change in fair value of warrant liability	(31,904)
Balance at December 31, 2009	626,492
Issuance of additional warrants	204,224
Change in fair value of warrant liability	282,103
Reclassification of warrant liability to stockholders equity	(1,112,819)
Balance at December 31, 2010	$

The fair value of the warrant liability is based on Level 3 inputs. For this liability, the Company developed its own assumptions that do not have observable inputs or available market data to support the fair value. See note 6(b) for further discussion of the warrant liability.

(c) Cash and Cash Equivalents

The Company considers all highly liquid debt instruments that have maturities of three months or less when acquired to be cash equivalents. As of December 31, 2010 and 2009, cash equivalents of $38,770,210 and $3,654,831, respectively, consisted of money market mutual funds invested in commercial paper and short-term corporate and government obligations. The Company s cash accounts are subject to account control agreements with certain lenders that give the lenders the right to assume control of the accounts in the event of a loan default (note 6).

(d) Property and Equipment

Property and equipment are recorded at cost and are depreciated on a straight-line basis over their estimated useful lives. The Company uses a life of three years for laboratory equipment and computer equipment, including software, and five years for office equipment and furniture. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset. Long-lived assets, such as property and equipment, are reviewed for

impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, then an impairment charge is recognized for the amount by which the carrying value of the asset exceeds the fair value of the asset. As of December 31, 2010 and 2009, management believes that no revision of the remaining useful lives or write-down of long-lived assets is required.

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(e) Government Grants

Grants received are recognized as revenue when the related work is performed and the qualifying research and development costs are incurred. In October 2010, the Company was awarded $649,959 in research grants by the U.S. government under the Qualifying Therapeutic Discovery Project program which was recognized as grant revenue for the year ended December 31, 2010.

(f) Research and Development and In-Process Research and Development

Research and development costs are charged to expense as incurred. Upfront and milestone payments made to third parties who perform research and development services on the Company s behalf will be expensed as services are rendered. Costs incurred in obtaining technology licenses are charged to research and development expense if the technology licensed has not reached technological feasibility and has no alternative future use.

(g) Income Taxes

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax basis and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

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(h) Stock-Based Compensation

The Company measures employee stock-based awards at grant date fair value and records compensation expense, net of expected forfeitures, if any, on a straight-line basis over the vesting period of the award. For stock-based awards that have performance based vesting criteria, compensation cost is recognized when it is deemed probable that the vesting criteria will be met.

Determining the appropriate fair value of stock-based awards requires the use of subjective assumptions, including, for stock options, the expected life of the option and expected stock price volatility, and, prior to the Company s initial public offering (IPO), the fair value of the Company s common stock. The Company uses the Black-Scholes option-pricing model to value its stock option awards. The assumptions used in calculating the fair value of stock-based awards represent management s best estimates and involve inherent uncertainties and the application of management s judgment. As a result, if factors change and management uses different assumptions, stock-based compensation expense could be materially different for future awards.

The expected life of stock options was estimated using the simplified method, as the Company has limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock option grants. The simplified method is the midpoint between the vesting period and the contractual term of the option. As a newly public company, sufficient history to estimate the expected life of stock options or the volatility of our common stock price is not available. The Company uses a basket of comparable public companies as a basis for the expected volatility assumption. The Company intends to continue to consistently apply this process using comparable companies until a sufficient amount of historical information regarding the volatility of the Company s share price becomes available.

Nonemployee awards are revalued until an award vests and compensation expense is recorded on a straight-line basis over the vesting period of each separate vesting tranche of the award, or using the accelerated attribution method. The estimation of the number of stock awards that will ultimately vest requires judgment, and to the extent actual results or updated estimates differ from the Company s current estimates, such amounts will be recorded as an adjustment in the period in which estimates are revised.

(i) Net Loss Per Common Share

Basic and diluted net loss per common share is determined by dividing net loss applicable to common stockholders by the weighted average common shares outstanding during the period. For all periods presented, the previously outstanding shares of Series A Convertible Preferred Stock (Series A) and Series B Convertible Preferred Stock (Series B), common stock options, unvested restricted stock and stock warrants have been excluded from the calculation because their effect would be anti-dilutive. Therefore, the weighted average shares used to calculate both basic and diluted loss per share are the same.

The following potentially dilutive securities have been excluded from the computations of diluted weighted average shares outstanding as of December 31, 2010, 2009 and 2008, as they would be anti-dilutive:

	December 31,		
	2010	**2009**	**2008**
Shares of redeemable convertible preferred stock		6,624,704	5,265,825
Shares issuable pursuant to redeemable convertible preferred stock accretion		912,285	451,233
Shares underlying outstanding options to purchase common stock	1,415,106	950,693	898,790
Shares of unvested restricted stock		8,887	70,640
Shares underlying outstanding warrants to purchase stock *	140,520	108,659	16,769

* The 2009 and 2008 amounts represent warrants to purchase preferred stock, the 2010 amount represents warrants to purchase common stock.

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(j) Segment Information

The Company is managed and operated as one business. The entire business is managed by a single management team that reports to the chief executive officer. The Company does not operate separate lines of business or separate business entities with respect to any of its product candidates. Accordingly, the Company does not prepare discrete financial information with respect to separate product areas and does not have separately reportable segments.

(k) Recently Issued Accounting Pronouncements

In January 2010, the FASB issued Accounting Standards Update (ASU) 2010-06, Fair Value Measurements and Disclosures (Topic 820): Improving Disclosures about Fair Value Measurements (ASU 2010-06), which amends the existing fair value measurement and disclosure guidance currently included in Accounting Standards Codification (ASC) Topic 820, Fair Value Measurements and Disclosures, to require additional disclosures regarding fair value measurements. Specifically, ASU 2010-06 requires entities to disclose the amounts of significant transfers between Level 1 and Level 2 of the fair value hierarchy and the reasons for these transfers, the reasons for any transfer in or out of Level 3 and information in the reconciliation of recurring Level 3 measurements about purchases, sales, issuances and settlements on a gross basis. In addition, ASU 2010-06 also clarifies the requirement for entities to disclose information about both the valuation techniques and inputs used in estimating Level 2 and Level 3 fair value measurements. ASU 2010-06 is effective for interim and annual reporting periods beginning after December 15, 2009, except for additional disclosures related to Level 3 fair value measurements, which are effective for fiscal years beginning after December 15, 2010. The adoption of ASU 2010-06 did not impact the Company s financial statements.

(l) Reverse Stock Split Ratio

On July 14, 2010, the board of directors of the Company approved a reverse stock split of the Company s common stock at a ratio of one share for every 8.0149 shares previously held. The stockholders approved the reverse stock split on July 19, 2010, and it was effected on July 20, 2010. All common stock share and per-share data included in these financial statements reflects the reverse stock split.

(4) Property and Equipment

Property and equipment consisted of the following:

	December 31,	
	2010	**2009**
Computer equipment and software	$ 179,126	$ 109,414
Office equipment and furniture	3,086	3,086
Lab equipment	19,623	19,623
Leasehold improvements	42,813	38,238
	244,648	170,361
Less accumulated depreciation and amortization	(146,382)	(99,733)
	$ 98,266	$ 70,628

Depreciation and amortization expense was $46,649, $57,383, and $48,197 for the years ended December 31, 2010, 2009 and 2008, respectively.

(5) Accrued Expenses

Accrued expenses consisted of the following:

	December 31,	
	2010	**2009**
Accrued compensation and benefits	$ 1,047,542	$ 504,091
Accrued professional fees	306,816	112,301
Accrued research and development expenses	1,502,330	238,401

Accrued interest and other	216,329	181,033
	$ 3,073,017	$ 1,035,826

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(6) Debt

(a) Convertible Notes

In July 2009, the Company issued convertible promissory notes for cash proceeds of $1,934,183 to existing investors, including two officers of the Company (the 2009 Notes). The 2009 Notes bore interest of 10% per year and were due on June 30, 2010, if not converted prior to such date, and were mandatorily convertible into preferred stock upon the occurrence of the Second Tranche Closing, as defined. The holders of the 2009 Notes were entitled to receive warrants to purchase shares of Series B upon the conversion of the 2009 Notes. The fair value of the warrants of $556,042 was recorded as a reduction in the carrying value of the 2009 Notes as original issue discount and recognized as interest expense during 2009. After the allocation of the original issue discount, the 2009 Notes contained a beneficial conversion feature (BCF) of $556,042, which was also recognized as additional interest expense during 2009.

In August 2009, the holders of the 2009 Notes converted their notes, including accrued interest of $22,840, into 2,104,326 shares of Series B at a conversion price of $0.93 per share. Upon conversion, the investors received warrants to purchase 736,514 shares of Series B at $0.93 per share which, upon completion of the Company s IPO, converted into warrants to purchase 91,890 shares of common stock at $7.45 per share that are exercisable for a term of up to seven years. The following table summarizes the fair value and the assumptions used for the Black-Scholes option-pricing model for the Series B warrants:

	December 31, 2009	Date of Issuance (August 20, 2009)
Fair value	$ 526,828	$ 556,042
Expected dividend yield	%	%
Expected volatility	87.83%	95.50%
Risk-free interest rate	3.26%	2.60%
Remaining contractual term	6.6 years	7 years

Upon the completion of the Company s IPO in August 2010, and as the result of these warrants converting into warrants to purchase common stock, they were reclassified into stockholder s equity.

In April 2010, the Company issued convertible promissory notes for cash proceeds of $10,062,500 to existing investors, including three officers of the Company (the April 2010 Convertible Notes). The April 2010 Convertible Notes bore interest of 8% per year and were due on December 31, 2010, if not converted prior to that date. The April 2010 Convertible Notes and related accrued interest were mandatorily convertible into common stock upon the completion of a qualifying IPO, at a conversion price equal to 80% of the offering price per share in such IPO. Upon the completion of the Company s IPO in August 2010, the April 2010 Convertible Notes and related accrued interest converted into 1,292,122 shares of common stock. The Company initially recorded the April 2010 Convertible Notes net of a $2,583,617 BCF, which has been fully recognized as interest expense as of December 31, 2010 as the result of the conversion of the April 2010 Convertible Notes.

(b) Credit Facilities and Vendor Debt

In May 2010, the Company executed a term loan facility with lenders to fund working capital needs. The loan is secured by a lien on all of the Company s assets, excluding intellectual property, which is subject to a negative pledge. The Company received proceeds of $5,000,000 at closing. An additional $6,000,000 of proceeds is available to the Company subject to final approval from the lenders. The loan bears interest at an annual rate of LIBOR plus 8.75%, subject to a LIBOR floor of 3.00%. The loan contains a material adverse change clause, as defined, which can trigger an event of default. In connection with the term loan facility, the Company s cash and investment accounts are subject to account control agreements with the lenders that give them the right to assume control of the accounts in the event of a loan default. The loan is repayable over 39 months with interest only payments for the first twelve months. As of December 31, 2010, the balance of the loan was $5,000,000, with $1,296,296 of that amount classified as current. In connection with the loan, the lenders received warrants to purchase 255,376 shares of Series B at $0.93 per share, which became warrants to purchase 31,861 shares of common stock at $7.45 per share upon the closing of the IPO.

The fair value of the warrants at the date of issuance of $204,224 has been recorded as deferred financing costs and will be amortized to interest expense through the maturity date of the debt. The Company is required to issue additional warrants to purchase up to an additional 38,235 shares of common stock in the event that additional proceeds are received from the lenders.

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In March 2007, the Company received a $2,500,000 loan from a finance company. The loan was secured by a lien on all of the Company s assets, excluding intellectual property, which was subject to a negative pledge. Interest on the loan was at a rate of 11.44%. The loan was interest-only for six months, and was repayable in equal monthly payments of principal and interest of $82,369 over 36 months. Interest expense of $42,633, $142,785 and $226,594 was recognized during the years ended December 31, 2010, 2009, and 2008 respectively. This loan was repaid on May 13, 2010. In connection with the loan from the finance company, the Company issued a warrant to purchase 134,408 shares of Series A at an exercise price of $0.93 per share, which became, upon the closing of the IPO, warrants to purchase 16,769 shares of common stock at an exercise price of $7.45 per share. The following table summarizes the fair value and the assumptions used for the Black-Scholes option-pricing model for the Series A warrants:

	December 31, 2009
Fair value	$ 99,664
Expected dividend yield	%
Expected volatility	89.17%
Risk-free interest rate	3.43%
Remaining contractual term	7.25 years

Upon the completion of the Company s IPO in August 2010, and as the result of these warrants converting into warrants to purchase common stock, they were reclassified into stockholder s equity.

Additionally, at December 31, 2010 and 2009, there was $216,571 and $36,043, respectively, outstanding on a short-term loan from an independent third party vendor.

(7) Capital Structure

(a) Initial Public Offering

In August 2010 the Company completed its initial public offering of common stock selling 5,000,000 shares at an offering price of $10.00 per share, resulting in gross proceeds of $50,000,000. Net proceeds after underwriting fees and offering expenses were approximately $43,000,000.

(b) Redeemable Convertible Preferred Stock

All outstanding shares of the Company s redeemable convertible preferred stock, plus accrued dividends thereon, were converted into 7,861,785 shares of common stock upon the completion of the IPO in August 2010.

(c) Warrants

All outstanding warrants to purchase shares of preferred stock converted into warrants to purchase an equal number of shares of common stock, adjusted for the reverse stock split as discussed in Note 3(l), upon completion of the IPO in August 2010. As of December 31, 2010, the following warrants to purchase common stock were outstanding:

	Number of Shares	Exercise Price	Expiration
Common Stock	140,520	$ 7.45	2016 through 2020

As of December 31, 2009, the warrants were classified as a warrant liability on the accompanying balance sheet as the warrants entitled the holder to purchase preferred stock, which could have been redeemed at the option of the holder. In connection with the Company s IPO, all outstanding warrants were reclassified into stockholders equity on the accompanying balance sheet as the warrants converted into warrants to purchase common stock.

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(8) Stock-Based Compensation

The Company is authorized to grant up to 1,738,886 shares of common stock under the NuPathe Inc. 2010 Omnibus Incentive Compensation Plan (the 2010 Plan). Such grants may be made to eligible employees, directors, consultants and advisors to the Company in the form of restricted stock, stock options, stock appreciation rights, stock units, performance units and other stock-based awards. The 2010 Plan was approved by stockholders in July 2010 and became effective on August 5, 2010. The 2010 Plan replaces the Company s 2005 Equity Compensation Plan (the 2005 Plan) and no further grants may be made under the 2005 Plan. All outstanding grants under the 2005 Plan shall be satisfied with shares under the 2010 Plan. Awards under the 2010 Plan are made by the Compensation Committee of the Company s board of directors. As of December 31, 2010, there were 314,893 shares of common stock available for future grants under the 2010 Plan.

Stock-based compensation expense for the years ended December 31, 2010, 2009 and 2008 includes compensation expense for employee (which also includes director) and nonemployee stock option grants and restricted stock grants. The compensation expense for the years ended December 31, 2010, 2009 and 2008 is as follows:

	Year Ended December 31,		
	2010	2009	2008
Stock options:			
Employee	$ 507,065	$ 308,418	$ 104,547
Nonemployee	27,751	18,869	9,466
	534,816	327,287	114,013
Restricted stock:			
Employee	8,534	(8,232)	44,163
	$ 543,350	$ 319,055	$ 158,176

The reversal of compensation expense for restricted stock in 2009 resulted from the forfeiture of restricted stock grants for which expense was recorded in prior years.

Stock-based compensation expense was included in the accompanying statements of operations for the years ended December 31, 2010, 2009 and 2008, as follows:

	Year Ended December 31,		
	2010	2009	2008
Research and development	$ 143,502	$ 118,504	$ 54,622
Selling, general and administrative	399,848	200,551	103,554
	$ 543,350	$ 319,055	$ 158,176

Stock Options

The weighted average fair value of the options granted during 2010, 2009 and 2008 was estimated at $6.36, $1.36 and $1.36, respectively, on the date of grant using the Black-Scholes option-pricing model with the following weighted average assumptions:

	Year Ended December 31,		
	2010	2009	2008
Expected dividend yield	%	%	%

Expected volatility	84.1%	92.8%	79.8%
Risk-free interest rate	1.9%	2.2%	2.9%
Expected life	6 years	5.25 years	6 years

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The following table summarizes the aggregate stock option activity:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term in Years	Aggregate Intrinsic Value
Outstanding at January 1, 2008	165,741	$ 1.28		
Granted	749,162	1.92		
Exercised	(155)	1.44		
Cancelled/forfeited	(15,958)	1.52		
Outstanding at December 31, 2008	898,790	1.76		
Granted	68,447	1.92		
Exercised				
Cancelled/forfeited	(16,544)	1.76		
Outstanding at December 31, 2009	950,693	1.81		
Granted	483,372	8.87		
Exercised	(4,878)	1.55		
Cancelled/forfeited	(14,081)	1.76		
Outstanding at December 31, 2010	1,415,106	$ 4.22	8.19	$ 7,138,997
Vested and expected to vest at December 31, 2010	1,415,106	$ 4.22	8.19	$ 7,138,997
Exercisable at December 31, 2010	629,902	$ 1.76	7.30	$ 4,596,937

Of the 483,372 stock options granted during 2010, 144,489 had performance-based vesting criteria. These 144,489 stock options were awarded to executive officers and include vesting criteria that are contingent upon the achievement of certain corporate milestones, as defined in the grant agreements. For stock-based awards that have performance-based vesting criteria, compensation cost is recognized when it is deemed probable that the vesting criteria will be met. As of December 31, 2010, the Company has not deemed the achievement of the vesting criteria to be probable, and therefore there has been no compensation expense recorded for these performance-based awards during 2010.

The aggregate intrinsic values represent the total amount by which the value of the shares of common stock subject to such options exceeds the exercise price of such options, based on the Company s closing stock price of $9.06 on December 31, 2010.

As of December 31, 2010, there was $3,256,376 of unrecognized compensation expense related to unvested stock options, which is expected to be recognized over a weighted average period of 2.6 years. As of December 31, 2010, there were a total of 1,104,084 in-the-money options.

The following table summarizes information about stock options outstanding at December 31, 2010:

	Options outstanding			Options exercisable	
			Weighted		Weighted

Exercise Price	Number of Options	average remaining contractual term (years)	Number of Options	average remaining contractual term (years)
$0.80	34,308	4.55	34,308	4.55
$0.96	16,217	5.07	16,217	5.07
$1.44	101,938	6.22	94,674	6.18
$1.92	779,271	7.78	484,703	7.79
$5.93	90,000	9.77		
$7.22	7,000	9.94		
$7.88	75,350	9.69		
$10.00	311,022	9.60		
	1,415,106	8.19	629,902	7.30

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Restricted Stock

The following table summarizes the aggregate restricted stock activity for the year ended December 31, 2010, 2009 and 2008:

	Number of Shares	Weighted Average Grant Date Fair Value
Nonvested shares at January 1, 2008	70,640	$ 1.36
Granted		
Vested		
Forfeited/repurchased		
Nonvested shares at December 31, 2008	70,640	$ 1.36
Granted		
Vested		
Forfeited/repurchased	(61,753)	$ 1.44
Nonvested shares at December 31, 2009	8,887	$ 0.96
Granted		
Vested	(8,887)	$ 0.96
Forfeited/repurchased		
Nonvested shares at December 31, 2010		

(9) Commitments

(a) Leases

The Company leases office space and office equipment under operating leases, which expire at various times through March 2013. Rent expense under these leases was $299,304, $299,342, and $316,350, for the years ended December 31, 2010, 2009 and 2008, respectively. Rent expense under these leases since inception was $1,219,130. Future minimum lease payments as of December 31, 2010 are as follows:

2011	$ 363,121
2012	368,228
2013	91,221
	$ 822,570

(b) License Agreements

In July 2008, the Company and Travanti Pharma Inc. (Travanti) entered into an asset purchase and license agreement and an assignment agreement. Pursuant to the terms of the Travanti agreement, the Company paid $5,500,000 for the purchase of a patent application, including all supporting documentation and priority documents that is directed to transdermal delivery of anti-migraine medications using an active delivery patch. The Company granted Travanti a nonexclusive, royalty-free, perpetual worldwide license to use the purchased patent application, and the invention covered by such patent application, outside the field of migraine. In addition, Travanti granted to the Company a perpetual, worldwide, exclusive, royalty-free license, with the right to grant sublicenses, under Travanti s patent rights and know-how that relate generally to specified iontophoresis technology to develop, make and commercialize migraine products. This fee was recognized in the accompanying statement of operations for the year ended December 31, 2008 as acquired in process research and development, as additional research and development efforts

and regulatory approval is required in order to commercialize this product in the United States.

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The Company entered into a patent license agreement with the University of Pennsylvania (Penn), which became effective in July 2006 and was amended in May 2007. Under the patent license agreement, Penn granted to the Company exclusive, worldwide rights under specified patent applications, and patents issuing therefrom, to make, use and sell products using Long Acting Delivery (LAD) technology. Under the agreement, the Company has the right to sublicense, subject to specified conditions, including the payment of sublicense fees. The patent license agreement requires that the Company use commercially reasonable efforts to develop and commercialize licensed products and requires the Company to commit a minimum of $250,000 per year towards such activities until the first commercial sale of the first licensed product. The license agreement requires the Company to make annual license maintenance payments of up to $50,000 to Penn until the first commercial sale of the first licensed product. The license agreement covers the Company s product candidates NP201 and NP202. In addition, the Company has agreed to pay Penn aggregate milestone payments of up to $950,000 upon the achievement of specified development and regulatory milestones related to each licensed product as specified and royalty payments equal to a specified percentage of future commercial sales of licensed products subject to the license through the expiration of the licensed patents. The Company paid annual license fees of $30,000, $30,000 and $20,000 in 2010, 2009 and 2008, respectively, which were recorded as research and development expense. The Company incurred expenses from Penn for $46,488, $64,864 and $72,984 in 2010, 2009 and 2008, respectively, for patent prosecution costs, which was recorded as expense by the Company.

In September 2009, the Company entered into a license agreement with SurModics Pharmaceuticals, Inc. (SurModics), pursuant to which the Company received an exclusive worldwide license, with the right to sublicense, under SurModics intellectual property, including its interest in joint inventions developed under a feasibility agreement, to make, have made, use, sell, import and export products covered by the license agreement. The Company granted SurModics an exclusive, perpetual, worldwide, royalty-free license under the Company s interest in joint inventions for uses that do not relate to products covered by the agreement or include any of the Company s existing technology or confidential information. The Company also granted SurModics a right of first negotiation to manufacture clinical supplies of covered products. If the Company and SurModics enter into such clinical manufacturing agreement, SurModics has a right of first negotiation to manufacture commercial supplies of covered products. The Company is obligated to pay aggregate milestones of up to $4,750,000 upon the achievement of specified development, regulatory and sales level milestones related to the first clinical indication approved by regulatory authority for covered products. The license agreement currently covers the Company s product candidate NP201. The Company must also pay an additional milestone payment upon regulatory approval of each additional clinical indication for covered products and specified royalties on sales of commercial product.

(c) Equipment Funding Agreement

In June 2010, the Company entered into an equipment funding agreement with LTS Lohmann Therapie-Systeme AG (LTS), under which the Company agreed to fund the purchase by LTS of manufacturing equipment for Zelrix, one of the Company s product candidates. The Company is required to make agreed upon installment payments to LTS, in the aggregate amount of 5,370,000 in 14 monthly installments that commenced in June 2010. As of December 31, 2010, 2,713,250, or approximately $3,595,500 based on exchange rates as of December 31, 2010, remains to be paid in accordance with monthly installments under the agreement. As of December 31, 2010, 2,656,750, or $3,410,315, based on exchange rates in effect at the time payments were made, has been recorded as a noncurrent asset in the accompanying balance sheet. Amounts capitalized under the LTS agreement will be amortized to cost of goods sold upon commencement of commercial sales of Zelrix.

Under the agreement, LTS will purchase and install the equipment according to an agreed upon project plan. LTS will own the purchased equipment and will be responsible for its routine and scheduled maintenance and repair. However, during the term of the LTS development and license agreement or any subsequent commercial manufacturing agreement that the parties may enter into, LTS will be required to use the purchased equipment solely for fulfilling its obligations to manufacture Zelrix. Additionally, during the term of the development and license agreement or such commercial manufacturing agreement, LTS is prohibited from encumbering the purchased equipment and may not sell or dispose of such equipment, except that LTS may transfer ownership of it to its affiliate, LTS Lohmann Therapy Systems Partnership L.P. If the Company does not enter into a commercial manufacturing agreement with LTS or if

the Company terminates the equipment funding agreement due to a breach by LTS, LTS must, at its option, either transfer ownership of the equipment to the Company or refund to the Company the purchase price of the equipment, less depreciation, as defined.

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The equipment funding agreement will remain in effect until the later of the completion by LTS of all installation activities or the execution of a commercial manufacturing agreement.

(d) Employment Agreements

Certain of the officers of the Company have employment agreements providing for severance and continuation of benefits in the event of termination without cause, including in the event of a Change of Control of the Company, as defined.

(10) 401(k) Profit Sharing Plan

The Company maintains a 401(k) Profit Sharing Plan (the 401(k) Plan) available to all employees meeting certain eligibility criteria. The 401(k) Plan permits participants to contribute up to 90% of their salary, not to exceed the limits established by the Internal Revenue Code. All contributions made by participants into the participants accounts vest immediately. Since 2008, the Company has provided a biweekly matching contribution to participant s accounts as provided for under the 401(k) Plan. This contribution is determined by a formula that is based on the employee s contributions, not to exceed 3% of their eligible wages, as defined by the 401(k) Plan. The Company sponsored match was $94,860, $74,425, and $61,565 for the years ended December 31, 2010, 2009 and 2008, respectively. The Company s contribution to the 401(k) Plan is 100% vested upon the contribution date.

(11) Related-Party Transactions

A former director of the Company, who resigned in July 2008, served as the chairman, through December 31, 2009, of a company that provides outsourced clinical development services to the pharmaceutical industry. During the year ended December 31, 2008, the Company purchased $166,308 of services from that company and its affiliates. The Company considers the fees paid fair value for the services rendered.

(12) Income Taxes

The Company sold $500,388 and $151,012 of Pennsylvania research and development tax credits to a third party buyer during the years ended December 31, 2010 and 2009, respectively. Accordingly, the Company recorded an income tax benefit of $500,388 and $151,012 for the years ended December 31, 2010 and 2009, respectively.

A reconciliation of the statutory U.S. federal rate to the Company s effective tax rate is as follows:

	Year Ended December 31,		
	2010	**2009**	**2008**
Percent of pre-tax income:			
U.S. federal statutory income tax rate	34.0%	34.0%	34.0%
State taxes, net of federal benefit	5.8	6.5	6.5
Other	(1.4)	1.0	3.8
Change in valuation allowance	(36.3)	(40.6)	(44.3)
Effective income tax rate	2.1%	0.9%	%

The tax effects of temporary differences that gave rise to significant portions of the deferred tax assets were as follows:

	December 31,	
	2010	**2009**
Net operating loss carryforwards	$ 25,702,568	$ 17,118,099
Research and development credit	1,627,895	1,272,271
Depreciation and amortization	1,899,425	2,014,476
Capitalized start-up costs	112,952	141,190
Other temporary differences	414,257	182,720
Gross deferred tax asset	29,757,097	20,728,756
Deferred tax assets valuation allowance	(29,757,097)	(20,728,756)

$ $

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In assessing the realizability of deferred tax assets, the Company considers whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible. Due to the Company s history of losses, the deferred tax assets are fully offset by a valuation allowance at December 31, 2010 and 2009. The valuation allowance in 2010 increased by $9,000,000 over 2009 and the valuation allowance in 2009 increased by $6,500,000 over 2008, related primarily to additional net operating losses incurred by the Company and additional capitalized start-up expenses.

As of December 31, 2010 and 2009, $278,000 and $348,000, respectively, of the Company s expenses had been capitalized for tax purposes as start-up costs. For tax purposes, capitalized start-up costs will be amortized over fifteen years beginning when the Company commences operations, as defined under the Internal Revenue Code.

The following table summarizes carryforwards of net operating losses and tax credits as of December 31, 2010:

	Amount	Expiration	
Federal net operating losses	$ 63,317,112	2026	2030
State net operating losses	63,317,112	2026	2030
Research and development credits	1,627,895	2025	2030

The Tax Reform Act of 1986 (the Act) provides for a limitation of the annual use of net operating loss and research and development tax credit carryforwards following certain ownership changes (as defined by the Act) that could limit the Company s ability to utilize these carryforwards. The Company has not completed a study to assess whether an ownership change has occurred, or whether there have been multiple ownership changes since its formation, due to the significant costs and complexities associated with such a study. The Company may have experienced various ownership changes, as defined by the Act, as a result of past financings. Accordingly, the Company s ability to utilize the aforementioned carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryforwards may be applied against future taxes; therefore, the Company may not be able to take full advantage of these carryforwards for federal or state income tax purposes.

On January 1, 2009, the Company adopted the provisions of Financial Accounting Standards Board (FASB) ASC 740-10, Accounting for Uncertainty in Income Taxes, which provides a financial statement recognition threshold and measurement attribute for a tax position taken or expected to be taken in a tax return. Under FASB ASC 740-10, the Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by taxing authorities, based solely on the technical merits of the position. The tax benefits recognized in the financial statements from such a position should be measured based on the largest benefit that has a greater than 50% likelihood to be sustained upon ultimate settlement. FASB ASC 740-10 also provides guidance on derecognition of income tax assets and liabilities, classification of current and deferred income tax assets and liabilities, accounting for interest and penalties associated with tax positions and income tax disclosures. The Company did not have unrecognized tax benefits as of December 31, 2010 and does not expect this to change significantly over the next twelve months. In connection with the adoption of FASB ASC 740-10, the Company will recognize interest and penalties accrued on any unrecognized tax benefits as a component of income tax expense. As of December 31, 2010, the Company has not accrued interest or penalties related to uncertain tax positions. The Company s tax returns for the years ended December 31, 2007 through December 31, 2010 are still subject to examination by major tax jurisdictions.

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(13) Quarterly Financial Information (unaudited)

This table summarizes the unaudited quarterly results of operations for the quarters in 2010 and 2009:

	2010 Results				
	First quarter	Second quarter	Third quarter	Fourth quarter	Total
Grant revenue	$	$	$	$ 649,959	$ 649,959
Operating expenses	4,262,935	4,213,153	6,510,958	6,848,439	21,835,485
Loss from operations	(4,262,935)	(4,213,153)	(6,510,958)	(6,198,480)	(21,185,526)
Interest expense, net	(10,487)	(1,431,301)	(2,073,688)	(155,173)	(3,670,649)
Loss before tax benefit	(4,273,422)	(5,644,454)	(8,584,646)	(6,353,653)	(24,856,175)
Income tax benefit	320,381			180,007	500,388
Net loss	(3,953,041)	(5,644,454)	(8,584,646)	(6,173,646)	(24,355,787)
Accretion of redeemable convertible preferred stock	(1,033,399)	(1,033,399)	(466,697)		(2,533,495)
Net loss available to common stockholders	$ (4,986,440)	$ (6,677,853)	$ (9,051,343)	$ (6,173,646)	$ (26,889,282)
Basic and diluted net loss per common share	$ (13.06)	$ (17.42)	$ (1.01)	$ (0.42)	$ (4.39)
Weighted average basic and diluted common shares outstanding	381,842	383,368	9,003,135	14,548,851	6,126,123

	2009 Results				
	First quarter	Second quarter	Third quarter	Fourth quarter	Total
Operating expenses	$ 3,792,190	$ 3,952,711	$ 3,445,573	$ 3,261,282	$ 14,451,756
Interest expense, net	(37,107)	(44,269)	(1,204,656)	(3,536)	(1,289,568)
Loss before tax benefit	(3,829,297)	(3,996,980)	(4,650,229)	(3,264,818)	(15,741,324)
Income tax benefit	151,012				151,012
Net loss	(3,678,285)	(3,996,980)	(4,650,229)	(3,264,818)	(15,590,312)

Accretion of redeemable convertible preferred stock	(829,766)	(829,766)	(924,280)	(1,033,399)	(3,617,211)
Net loss available to common stockholders	$ (4,508,051)	$ (4,826,746)	$ (5,574,509)	$ (4,298,217)	$ (19,207,523)
Basic and diluted net loss per common share	$ (11.81)	$ (12.64)	$ (14.60)	$ (11.26)	$ (50.31)
Weighted average basic and diluted common shares outstanding	381,789	381,789	381,789	381,789	381,789

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ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Annual Report, the effectiveness of our disclosure controls and procedures. Based on that evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level in ensuring that information required to be disclosed by us in the reports that we file or submit under the Securities Exchange Act of 1934, as amended, or the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

Management s Report on Internal Control Over Financial Reporting

This annual report does not include a report of management s assessment regarding internal control over financial reporting or an attestation report of the company s registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Changes to Internal Controls Over Financial Reporting

There has been no change in internal controls over financial reporting that occurred during the period covered by this report that has materially affected, or is reasonably likely to materially affect, the company s internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

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PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees. Our Code of Business Conduct and Ethics contains provisions that satisfy the standards for a code of ethics set forth in Item 406 of Regulation S-K of the rules and regulations of the SEC. Our Code of Business Conduct and Ethics also contains a special code of ethics that is applicable to our Chief Executive Officer and our senior financial officers. Our Code of Business Conduct and Ethics is available through our website s Investor Relations - Corporate Governance page, the address of which is www.nupathe.com.

To the extent that we amend any provision of our Code of Conduct or grant a waiver from any provision of our Code of Conduct that is applicable to any of our directors or our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions, we intend to satisfy our disclosure obligations under applicable SEC rules by posting such information on our Internet Web site under the heading For Investors Corporate Governance.

The reference to our website is intended to be inactive textual references only, and the contents of our websites is not incorporated by reference herein.

The additional information required by this item is incorporated herein by reference to the sections captioned Election of Directors, Executive Officers, Corporate Governance, and Section 16(a) Beneficial Ownership Reporting Compliance in our definitive Proxy Statement relating to our 2011 Annual Meeting of Stockholders.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated herein by reference to the section captioned Executive Compensation in our definitive Proxy Statement relating to our 2011 Annual Meeting of Stockholders.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item is incorporated herein by reference to the sections captioned Security Ownership of Certain Beneficial Owners and Management and Equity Compensation Plan Information in our definitive Proxy Statement relating to our 2011 Annual Meeting of Stockholders.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is incorporated herein by reference to the section captioned Director Independence and Relationships and Related Party Transactions in our definitive Proxy Statement relating to our 2011 Annual Meeting of Stockholders.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item is incorporated herein by reference to the section captioned Ratification of Selection of Independent Registered Public Accounting Firm in our definitive Proxy Statement relating to our 2011 Annual Meeting of Stockholders.

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PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

Financial Statements: The following financial statements are included in Part II, Item 8 of this Form 10-K:

Financial Statement Schedules: All schedules to our financial statements are omitted because they are not applicable or not required, or because the required information is included in the financial statements or notes thereto.

Exhibits: A list of exhibits filed as part of this Form 10-K is set forth in the Exhibit Index that immediately follows the signature page to this Form 10-K and is incorporated by reference herein. Where so indicated by footnote, exhibits which were previously filed are incorporated by reference.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

NUPATHE INC.

Date: March 18, 2011

By: /s/ Jane H. Hollingsworth
Jane H. Hollingsworth
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Jane H. Hollingsworth and Keith A. Goldan, jointly and severally, his or her attorney-in-fact, with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Report and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Report has been signed by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Jane H. Hollingsworth Jane H. Hollingsworth	Chief Executive Officer and Director (*Principal Executive Officer*)	March 18, 2011
/s/ Keith A. Goldan Keith A. Goldan	Chief Financial Officer (*Principal Financial and Accounting Officer*)	March 18, 2011
/s/ Wayne P. Yetter Wayne P. Yetter	Chairman of the Board	March 18, 2011
/s/ Michael Cola Michael Cola	Director	March 18, 2011
/s/ Jeanne Cunicelli Jeanne Cunicelli	Director	March 18, 2011
/s/ Michael C. Diem Michael C. Diem, M.D.	Director	March 18, 2011
/s/ William J. Federici William J. Federici	Director	March 18, 2011

/s/ Richard S. Kollender	Director	March 18, 2011
Richard S. Kollender		
/s/ Gary J. Kurtzman	Director	March 18, 2011
Gary J. Kurtzman, M.D.		
/s/ Robert P. Roche, Jr.	Director	March 18, 2011
Robert P. Roche, Jr.		

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INDEX TO EXHIBITS

Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
3.1	Restated Certificate of Incorporation of NuPathe Inc.	8-K	001-34836	3.1	August 12, 2010	
3.2	Bylaws of NuPathe Inc.	8-K	001-34836	3.2	August 12, 2010	
4.1	Amended and Restated Investor Rights Agreement, dated as of July 8, 2008, as amended on July 20, 2010 and August 4, 2010	S-1/A	333-166825	4.1	August 5, 2010	
4.2	Preferred Stock Warrant, dated as of March 29, 2007, as amended, issued to Oxford Finance Corp.	S-1/A	333-166825	4.2	June 15, 2010	
4.3	Form of Warrant to Purchase Shares of Series B Preferred Stock, as amended	S-1/A	333-166825	4.3	June 15, 2010	
4.4	Series B Preferred Stock Warrant, dated May 13, 2010, issued to MidCap Funding III, LLC	S-1/A	333-166825	4.4	June 15, 2010	
4.5	Series B Preferred Stock Warrant, dated May 13, 2010, issued to Silicon Valley Bank	S-1/A	333-166825	4.5	June 15, 2010	
10.1*	Patent License Agreement, effective as of July 1, 2006, as amended, between NuPathe Inc. and The Trustees of the University of Pennsylvania	S-1/A	333-166825	10.1	June 15, 2010	
10.2*	Development and License Agreement, dated September 14, 2007, as amended, between NuPathe Inc. and LTS Lohmann Therapie-Systeme AG	S-1/A	333-166825	10.2	July 27, 2010	
10.3	Asset Purchase and License Agreement, dated July 8, 2008, between NuPathe Inc. and Travanti Pharma Inc.	S-1/A	333-166825	10.3	June 15, 2010	
10.4*	Feasibility Evaluation Agreement, dated March 19, 2007, as amended,	S-1/A	333-166825	10.4	July 27, 2010	

	between NuPathe Inc. and SurModics Pharmaceuticals, Inc. (f/k/a Brookwood Pharmaceuticals, Inc.)				
10.5*	License Agreement, dated September 23, 2009, between NuPathe Inc. and SurModics Pharmaceuticals, Inc. (f/k/a Brookwood Pharmaceuticals, Inc.)	S-1/A	333-166825	10.5	July 27, 2010
10.6	Secured Subordinated Convertible Note and Warrant Purchase Agreement, dated April 9, 2010, between NuPathe Inc. and the Purchasers named therein	S-1/A	333-166825	10.6	June 15, 2010
10.7	Loan and Security Agreement, effective as of May 13, 2010, by and among MidCap Funding III, LLC, Silicon Valley Bank and NuPathe Inc.	S-1/A	333-166825	10.7	June 15, 2010
10.8	Secured Promissory Note, dated May 13, 2010, made by NuPathe Inc. in favor of MidCap Funding III, LLC	S-1/A	333-166825	10.8	June 15, 2010

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Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
10.9	Secured Promissory Note, dated May 13, 2010, made by NuPathe Inc. in favor of Silicon Valley Bank	S-1/A	333-166825	10.9	June 15, 2010	
10.10*	Equipment Funding Agreement, dated June 1, 2010, between NuPathe Inc. and LTS Lohmann Therapie-Systeme AG	S-1/A	333-166825	10.11	July 27, 2010	
10.11	Office Space Lease, dated January 10, 2008, between NuPathe Inc. and Washington Street Associates II, L.P.	S-1/A	333-166825	10.10	June 15, 2010	
10.12	First Amendment to Office Space Lease, dated November 1, 2010, between NuPathe Inc. and Washington Street Associates II, L.P.					X
10.13#	Amended and Restated 2005 Equity Compensation Plan, as amended, including forms of Incentive Stock Option Grant, Nonqualified Stock Option Grant and Restricted Stock Grant Agreement thereunder	S-1/A	333-166825	10.12	June 15, 2010	
10.14#	NuPathe Inc. 2010 Omnibus Incentive Compensation Plan	10-Q	001-34836	10.1	November 12, 2010	
10.15#	Form of Incentive Stock Option Grant Agreement for awards under NuPathe Inc. 2010 Omnibus Incentive Compensation Plan	10-Q	001-34836	10.2	November 12, 2010	
10.16#	Form of Nonqualified Stock Option Grant Agreement for awards under NuPathe Inc. 2010 Omnibus Incentive Compensation Plan	10-Q	001-34836	10.3	November 12, 2010	
10.17#	Form of Nonqualified Stock Option Grant Agreement for awards to non-employee directors under NuPathe Inc. 2010 Omnibus Incentive Compensation Plan	10-Q	001-34836	10.4	November 12, 2010	

10.18#	Form of Restricted Stock Grant Agreement for awards under NuPathe Inc. 2010 Omnibus Incentive Compensation Plan	10-Q	001-34836	10.5	November 12, 2010	
10.19#	NuPathe Inc. 2010 Employee Stock Purchase Plan	S-1/A	333-166825	10.14	July 21, 2010	
10.20#	Employment Agreement between NuPathe Inc. and Jane H. Hollingsworth	S-1/A	333-166825	10.15	July 9, 2010	
10.21#	Employment Agreement between NuPathe Inc. and Terri B. Sebree	S-1/A	333-166825	10.16	July 9, 2010	
10.22#	Employment Agreement between NuPathe Inc. and Keith A. Goldan	S-1/A	333-166825	10.17	July 9, 2010	
10.23#	Employment Agreement between NuPathe Inc. and Gerald W. McLaughlin	S-1/A	333-166825	10.18	July 9, 2010	
10.24#	Employment Agreement between NuPathe Inc. and Ezra H. Felker	S-1/A	333-166825	10.19	July 9, 2010	
10.25#	Employment Agreement, dated October 7, 2010, by and between NuPathe Inc. and Michael F. Marino	10-Q	001-34836	10.8	November 12, 2010	
10.26#	NuPathe Inc. Non-employee Director Compensation Policy					X

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Exhibit Number	Exhibit Description	Incorporated by Reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
10.27#	Form of Director Indemnification Agreement	S-1/A	333-166825	10.20	July 9, 2010	
10.28#	List of current directors with a Director Indemnification Agreement in the form provided as Exhibit 10.27					X
10.29	License Agreement, dated December 1, 2010 between NuPathe Inc. and Washington Street Associates II, L.P.					X
23.1	Consent of KPMG LLP, independent registered public accounting firm					X
24.1	Power of Attorney (included in the signature page to this Form 10-K)					X
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14 (a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
32.1	Certification by Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					

* Certain information in this exhibit has been omitted pursuant to an Order Granting Confidential Treatment issued by the Securities and Exchange Commission.

\# Indicates management contract or compensatory plan or arrangement.

Furnished herewith.