NUPATHE INC.
Form S-1/A
August 02, 2010

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As filed with the Securities and Exchange Commission on August 2, 2010
Registration No. 333-166825

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

Amendment No. 5
to
Form S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

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

Delaware	**2834**	**20-2218246**
(State or other jurisdiction of incorporation or organization)	*(Primary Standard Industrial Classification Code Number)*	*(I.R.S. Employer Identification Number)*

227 Washington Street, Suite 200
Conshohocken, Pennsylvania 19428
(484) 567-0130
(Address, including zip code and telephone number, including area code, of registrant s principal executive offices)

Jane H. Hollingsworth
Chief Executive Officer
NuPathe Inc.
227 Washington Street, Suite 200
Conshohocken, Pennsylvania 19428

(484) 567-0130

(Name, address, including zip code and telephone number, including area code, of agent for service)

Copies to:

Michael N. Peterson, Esq. **James W. McKenzie, Jr., Esq.** **Morgan, Lewis & Bockius LLP** **1701 Market Street** **Philadelphia, Pennsylvania 19103** **(215) 963-5000**	**Suzanne M. Hanlon, Esq.** **V.P. Administration, General Counsel, Secretary** **NuPathe Inc.** **227 Washington Street, Suite 200** **Conshohocken, Pennsylvania 19428** **(484) 567-0130**	**David E. Redlick, Esq.** **Brian A. Johnson, Esq.** **Wilmer Cutler Pickering Hale and Dorr LLP** **399 Park Avenue** **New York, New York 10022** **(212) 230-8800**

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

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

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

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is declared effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED AUGUST 2, 2010

PROSPECTUS

5,000,000 Shares

Common Stock

NuPathe Inc. is offering 5,000,000 shares of common stock. This is our initial public offering, and no public market currently exists for our common stock. We anticipate that the initial public offering price will be between $14.00 and $16.00 per share.

We have applied to have our common stock listed on The NASDAQ Global Market under the symbol PATH.

Investing in our common stock involves risks. See Risk Factors beginning on page 8.

	Per Share	Total
Initial public offering price	$	$
Underwriting discounts and commissions	$	$
Proceeds, before expenses, to us	$	$

We have granted the underwriters an option for 30 days from the date of this prospectus to purchase up to 750,000 additional shares of our common stock at the initial public offering price, less underwriting discounts and commissions, to cover over-allotments.

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

The underwriters expect to deliver the shares of common stock on or about , 2010.

Leerink Swann **Lazard Capital Markets**

Needham & Company, LLC

The date of this prospectus is , 2010.

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You should rely only on the information contained in this prospectus and any free writing prospectus prepared by or on behalf of us or to which we have referred you. We have not authorized anyone to provide you with information that is different. We are offering to sell shares of our common stock, and seeking offers to buy shares of our common stock, only in jurisdictions where offers and sales are permitted. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock.

Until , 2010, 25 days after the date of this prospectus, all dealers that buy, sell or trade our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealer s obligation to deliver a prospectus when acting as an underwriter and with respect to unsold allotments or subscriptions.

For investors outside the United States: Neither we nor any of the underwriters have taken any action to permit a public offering of the shares of our common stock or the possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. Before you decide to invest in our common stock, you should read the entire prospectus carefully, including the Risk Factors section and the financial statements and related notes appearing at the end of this prospectus.

Our Company

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 a single-use patch applied to the arm or thigh for the treatment of migraine. Zelrix actively delivers sumatriptan through the skin in a controlled manner using our proprietary SmartRelief technology. Sumatriptan, currently available in oral, nasal and injectable formulations, is the most widely prescribed migraine medication. We designed Zelrix for patients who suffer from nausea or vomiting with migraines and for those who experience inconsistent relief or adverse events from their current treatment.

We successfully completed a pivotal Phase III clinical trial for Zelrix in July 2009 and expect to submit a New Drug Application, or NDA, to the United States Food and Drug Administration, or FDA, in the fourth quarter of 2010. Subject to FDA approval of our NDA, we plan to build our own specialty sales force in the U.S. to launch Zelrix in the first half of 2012.

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, or IND, to the FDA in the first half of 2011 for NP201 and in 2012 for NP202 in order to initiate human clinical trials of these product candidates.

Our Product Candidates

Zelrix for the treatment of acute migraine

Migraine is a debilitating neurological disease that affects approximately 28 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. 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 and prevent or discourage migraine patients, or migraineurs, from taking their migraine medication.

According to IMS Health Inc., or IMS, a leading provider of pharmaceutical industry market data, over 13 million prescriptions for the treatment of acute migraine were filled in the U.S. in 2009, with more than 90% of these prescriptions for triptans. Triptan sales in the U.S. in 2009 exceeded $2.0 billion, with approximately 123 million individual units sold. Currently, triptans constitute the most prescribed class of medication for the treatment of acute migraine, and sumatriptan is the most widely prescribed triptan.

We believe that most marketed migraine therapies have significant limitations. Zelrix is a transdermal patch designed to provide migraineurs fast onset and sustained relief through a tolerable, non-oral route of administration. We believe

Zelrix offers a better alternative to migraineurs by providing the following benefits:

Circumventing nausea and vomiting. According to a survey of over 500 respondents conducted by the National Headache Foundation in 2008, 90% of migraineurs have experienced nausea with a migraine and 59% of migraineurs have experienced vomiting with a migraine. In this survey, 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. The American Academy of Neurology guidelines recommend non-oral therapies for migraineurs who experience nausea or vomiting as significant migraine symptoms. Because Zelrix is administered transdermally, we believe

that it will be attractive to migraineurs suffering from nausea or vomiting who might otherwise delay or avoid taking medication.

Increasing consistency of response. 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. We believe this results from a variety of causes, including low and inconsistent absorption of oral medication because of a compromised ability to digest, or decreased gastric motility. Because Zelrix does not depend on gastrointestinal absorption, we believe that it will provide more consistent relief than oral triptans.

Minimizing triptan adverse events. According to a 2003 article by Dr. R. Michael Gallagher published in *Headache*, a peer-reviewed medical journal, 67% of migraineurs who use prescription migraine medication reported that they had delayed or avoided taking a prescription migraine medication due to concerns about adverse events. In our clinical trials, treatment with Zelrix resulted in a low incidence of triptan adverse events while effectively treating migraine.

We plan to develop marketing, sales and distribution capabilities for the commercial launch of Zelrix in the U.S., including the hiring of a specialty sales force of approximately 100 people after marketing approval. We expect to direct our marketing efforts to high potential prescribers of Zelrix, including neurologists, headache specialists and select primary care physicians. We may seek to further penetrate the U.S. market in the future by expanding our sales force or through collaborations with other pharmaceutical and biotechnology companies. We may also seek to commercialize Zelrix outside the U.S., although we currently plan to do so only with a partner.

NP201 for the continuous symptomatic treatment of Parkinson s disease

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. Symptoms of Parkinson s disease can appear at any age, but the average age of onset is 60. According to IMS, 2009 sales of Parkinson s disease therapies in the U.S., European Union and Japan totaled approximately $3.6 billion.

We designed NP201 to provide continuous delivery of Parkinson s disease medication in an easy to administer and tolerable dose formulation. After administration, NP201 is designed to slowly release ropinirole, an FDA approved medication. Based on data from our preclinical studies, we believe that 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. We plan to submit an IND to the FDA in the first half of 2011.

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

According to the National Alliance on Mental Illness, in the U.S., schizophrenia affects over two million adults and bipolar disorder affects over ten million adults. In an attempt to improve patient compliance, physicians currently administer antipsychotic drugs through depot injections, which release medication over a longer period than conventional injections or oral medications.

We designed NP202 to provide continuous delivery of an FDA approved atypical antipsychotic medication in an easy to administer and tolerable dose formulation. We believe that NP202 will provide a significant improvement over existing treatment options because we are designing and developing it to deliver up to three months of continuous medication with a single dose and be an easy to administer, pre-loaded, injectable product that can be stored at room temperature. 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

We hold exclusive worldwide rights to two proprietary drug delivery technologies: SmartRelief and LAD. Zelrix uses SmartRelief, while NP201 and NP202 both use our long-acting delivery, or LAD, technology.

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SmartRelief is our proprietary transdermal delivery technology based on iontophoresis, a non-invasive method of transporting a molecule through the skin by applying a mild electrical current. Unlike passive transdermal technologies, which rely on diffusion for medication delivery, SmartRelief controls the amount and rate of medication delivery. The SmartRelief technology facilitates active transdermal delivery, which is important for molecules, such as sumatriptan, that are not able to be delivered passively through the skin.

LAD is comprised of a biodegradable polymer matrix using commonly available medical polymers and an active drug. It is formed into a small implant for injection just below the skin. We designed LAD to improve the control, consistency and convenience of medication delivery.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are described in more detail in the Risk Factors section of this prospectus immediately following this prospectus summary. These risks include the following:

- We have not received, and we may not receive, marketing approval for, or commercial revenues from, Zelrix or any other product candidate;
- The commercial success of Zelrix and any other product candidate that we develop, if approved, will depend upon significant market acceptance among physicians and patients and the availability of adequate reimbursement from third party payors;
- If we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to perform these functions, we will not be able to commercialize Zelrix or any other product candidate that we develop, if approved;
- We have incurred significant operating losses since inception, which has raised substantial doubt regarding our ability to continue as a going concern; and
- 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.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in January 2005. Our principal executive offices are located at 227 Washington Street, Suite 200, Conshohocken, Pennsylvania 19428 and our telephone number is (484) 567-0130. Our website address is www.nupathe.com. The information contained on, or that can be accessed through, our website is not part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

In this prospectus, unless otherwise stated or the context otherwise indicates, references to NuPathe, we, us, our and similar references refer to NuPathe Inc. The name NuPathe® is our registered trademark. Zelrix™, SmartRelief™ and LAD™ are our trademarks. All other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

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THE OFFERING

Common stock offered by us	5,000,000 shares
Common stock to be outstanding after this offering	14,112,231 shares
Over-allotment option	We have granted the underwriters an option for 30 days from the date of this prospectus to purchase up to 750,000 additional shares of common stock to cover over-allotments.
Use of proceeds	We intend to use the net proceeds from this offering to complete the clinical development of, seek marketing approval for and, if approved, commercially launch Zelrix in the U.S., to continue preclinical and clinical development of NP201 and NP202 and for working capital and other general corporate purposes. See Use of Proceeds on page 34.
Proposed NASDAQ Global Market symbol	PATH
Risk factors	You should read the Risk Factors section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.

The number of shares of common stock to be outstanding after this offering is based on 392,254 actual shares of common stock outstanding as of June 30, 2010 and also includes:

- 7,858,934 shares of common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock, including accrued dividends, upon the closing of this offering, assuming that the closing occurs on August 9, 2010; and

- 861,043 shares of common stock issuable upon the automatic conversion of all principal and accrued interest outstanding under secured subordinated promissory notes that we issued and sold to investors in April 2010, or the April 2010 Convertible Notes, upon the closing of this offering, assuming an initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and that the closing occurs on August 9, 2010.

The number of shares of common stock to be outstanding after this offering excludes:

- 938,223 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2010 at a weighted average exercise price of $1.81 per share;

- 345,350 shares of common stock issuable upon the exercise of options, to be granted effective upon the effective date of the registration statement for this offering, at an exercise price equal to the initial public offering price;

140,520 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2010 at a weighted average exercise price of $7.45 per share; and

791,776 additional shares of common stock reserved for future issuance under our 2010 Omnibus Incentive Compensation Plan, or our 2010 Plan, which will become effective upon the effective date of the registration statement for this offering, including 105,555 shares of common stock reserved for issuance as of June 30, 2010 under our 2005 Equity Compensation Plan, or our 2005 Plan, which shares will be added to the shares reserved for future issuance under our 2010 Plan upon effectiveness of our 2010 Plan.

Unless otherwise indicated, all information in this prospectus assumes:

No exercise of the outstanding options or warrants described above;

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No exercise by the underwriters of their option to purchase up to 750,000 shares of common stock to cover over-allotments;

The automatic conversion of all outstanding shares of our preferred stock, including accrued dividends, into an aggregate of 7,858,934 shares of common stock upon the closing of this offering, assuming that the closing occurs on August 9, 2010;

The automatic conversion of all principal and accrued interest outstanding under the April 2010 Convertible Notes into an aggregate of 861,043 shares of common stock upon the closing of this offering, assuming an initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and that the closing occurs on August 9, 2010;

The warrants outstanding as of June 30, 2010 to purchase an aggregate of 1,126,298 shares of preferred stock have become, in accordance with their terms, warrants to purchase 140,520 shares of common stock at an exercise price of $7.45 per share of common stock upon the closing of this offering; and

The restatement of our amended and restated certificate of incorporation and our bylaws upon the closing of this offering.

In addition, unless otherwise indicated, all information in this prospectus gives effect to the one-for-8.0149 reverse stock split of common stock that was effected on July 20, 2010.

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SUMMARY FINANCIAL DATA

You should read the following summary financial data together with the Capitalization, Selected Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations sections of this prospectus and our financial statements and the related notes appearing at the end of this prospectus. We have derived the statement of operations data for the years ended December 31, 2007, 2008 and 2009 from our audited financial statements appearing at the end of this prospectus. We have derived the statement of operations data for the three months ended March 31, 2009 and 2010 and for the period from January 7, 2005 (inception) through March 31, 2010 and the balance sheet data as of March 31, 2010 from our unaudited financial statements appearing at the end of this prospectus. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period and our interim period results are not necessarily indicative of results for a full year.

See note 3(j) to our financial statements appearing at the end of this prospectus for information regarding computation of basic and diluted net loss per common share, unaudited pro forma basic and diluted net loss per common share and the unaudited pro forma weighted average basic and diluted common shares outstanding used in computing pro forma basic and diluted net loss per common share.

The unaudited pro forma balance sheet data set forth below give effect to:

- The automatic conversion of all outstanding shares of our preferred stock, including accrued dividends, into an aggregate of 7,858,934 shares of common stock upon the closing of this offering, assuming that the closing occurs on August 9, 2010;

- The receipt in April 2010 of gross proceeds of $10,062,500 upon the issuance of the April 2010 Convertible Notes and the automatic conversion of all principal and accrued interest outstanding under the April 2010 Convertible Notes into an aggregate of 861,043 shares of common stock upon the closing of this offering, assuming an initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and that the closing occurs on August 9, 2010;

- The receipt in May 2010 of gross proceeds of $5,000,000 upon entering into a secured term loan facility, or the May 2010 Loan Facility, the issuance of warrants to purchase 255,376 shares of Series B preferred stock, with an estimated fair value of $203,255, to the lenders under such facility and the repayment in full of the $555,208 outstanding as of March 31, 2010 under a term loan that we entered into in 2007; and

- The warrants outstanding as of June 30, 2010 to purchase an aggregate of 1,126,298 shares of our preferred stock becoming, in accordance with their terms, warrants to purchase 140,520 shares of common stock at an exercise price of $7.45 per share of common stock upon the closing of this offering and the reclassification of the warrant liability with respect to warrants outstanding as of March 31, 2010 to additional paid-in capital.

The pro forma as adjusted balance sheet data set forth below give further effect to the issuance and sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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	Year Ended December 31,			Three Months Ended March 31,		January 7, 2005 (inception) through March 31,
	2007	2008	2009	2009	2010	2010
				(Unaudited)		(Unaudited)
	(In thousands, except share and per share data)					
Statement of Operations Data:						
Operating expenses:						
Research and development	$ 7,761	$ 8,815	$ 11,310	$ 2,996	$ 3,390	$ 35,178
Acquired in-process research and development		5,500				5,500
General and administrative	1,884	3,075	3,142	796	873	10,700
Total operating expenses	(9,645)	(17,390)	(14,452)	(3,792)	(4,263)	(51,378)
Interest income (expense), net	(30)	(121)	(1,289)	(37)	(10)	(2,106)
Loss before tax benefit	(9,675)	(17,511)	(15,741)	(3,829)	(4,273)	(53,484)
Income tax benefit			151	151	320	471
Net loss	(9,675)	(17,511)	(15,590)	(3,678)	(3,953)	$ (53,013)
Accretion of redeemable convertible preferred stock	(1,126)	(2,330)	(3,617)	(830)	(1,033)	
Net loss applicable to common stockholders	$ (10,801)	$ (19,841)	$ (19,207)	$ (4,508)	$ (4,986)	
Basic and diluted net loss per common share	$ (29.38)	$ (51.98)	$ (50.31)	$ (11.81)	$ (13.06)	
Weighted average basic and diluted common shares outstanding	367,691	381,681	381,789	381,789	381,842	
Unaudited pro forma net loss			$ (15,590)		$ (3,953)	
Unaudited pro forma basic and diluted net loss per common share			$ (2.04)		$ (0.45)	
Unaudited pro forma weighted average basic and			7,654,193		8,823,612	

diluted common shares outstanding

	As of March 31, 2010		
	Actual	Pro Forma (Unaudited) (In thousands)	Pro Forma as Adjusted
Balance Sheet Data:			
Cash and cash equivalents	$ 592	$ 15,100	$ 81,550
Working capital	(2,372)	12,691	79,141
Total assets	1,580	16,290	82,740
Long-term debt		5,000	5,000
Redeemable convertible preferred stock	56,572		
Total stockholders equity (deficit)	(59,390)	8,053	74,503

Each $1.00 increase or decrease in the assumed initial public offering price of $15.00 per share would increase or decrease each of cash and cash equivalents, working capital, total assets and total stockholders equity on a pro forma as adjusted basis by approximately $4.6 million, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should consider carefully the risks described below, together with the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus. We believe the risks described below are the risks that are material to us as of the date of this prospectus. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

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. In the fourth quarter of 2010, we plan to submit a new drug application, or NDA, 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, Zelrix is still, nonetheless, susceptible to the risks of failure inherent at any stage of drug development, including the appearance of unexpected adverse events and the FDA s determination Zelrix is not approvable. If we do not receive FDA approval for and commercialize Zelrix, we will not be able to generate product revenues in the foreseeable future, or at all.

As a company, we have never obtained marketing approval for or commercialized a drug. It is possible that the FDA may refuse to accept our NDA for substantive review or may review our data and conclude that our application is insufficient to obtain marketing approval of Zelrix. Before we submit our NDA, we must complete two ongoing pharmacokinetic trials in healthy subjects and submit interim safety data from our two ongoing open label Phase III long-term safety trials, or our Phase III safety trials.

In addition, in July 2010, the FDA notified us that the skin sensitization data being collected during our two Phase III safety trials has the potential to be sufficient, subject to review by the FDA as part of the NDA for Zelrix, without the need to conduct a separate skin sensitization study. Depending on the outcome of the FDA s review, we may be required to conduct the separate skin sensitization study. The FDA also has requested that we provide data in our NDA regarding an *in vitro* analytical testing method for Zelrix. However, to date, for technical reasons we have not been able to develop an appropriate *in vitro* analytical testing method for Zelrix, and we are working with the FDA to develop acceptable alternatives.

Any difficulties or delays we experience in obtaining the data from our pharmacokinetic and Phase III safety trials will delay the submission of our NDA and the FDA s review of the NDA. In addition, if the FDA requires a separate skin sensitization study or if we are delayed in developing or fail to develop an *in vitro* analytical testing method for Zelrix, or are delayed in reaching or fail to reach agreement with the FDA on an alternative, marketing approval of Zelrix may be delayed.

If, following submission, our NDA is not accepted for substantive review or approved, the FDA may require that we conduct additional clinical or preclinical trials, manufacture additional validation batches or develop additional analytical test methods before it will reconsider 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 and analytical testing methods support marketing approval of Zelrix in the U.S., the FDA may not agree with our analysis and approve our NDA. Any delay in

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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;
- 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.

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.

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 current plan is to hire most of our 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 is sumatriptan, with 2009 sales of approximately $800 million in the U.S., including approximately $200 million attributable to GlaxoSmithKline plc s, or GlaxoSmithKline, branded sumatriptan, Imitrex. There are at least eight other branded triptan therapies being sold by pharmaceutical and biotechnology companies, including Maxalt from Merck & Co., Inc., or Merck, and Treximet from GlaxoSmithKline. In July 2009, the FDA approved Zogenix, Inc. s Sumavel DosePro needle-free sumatriptan injection for the treatment of acute migraine and cluster headache, and 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. 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 likely would require or encourage use of, and consumers likely would use, a generic triptan prior to trying Zelrix.

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, and Allergan, Inc. s Botox for chronic migraine. Each of these has either completed or is in Phase III clinical development. Zelrix may also compete with other drug candidates that receive marketing approval before Zelrix. 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

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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;
- 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 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 pharmacokinetic and Phase III safety trials required for our NDA submission for Zelrix.

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.

Even if Zelrix receives FDA marketing approval, we may not be able to secure marketing exclusivity in the U.S.

Although we plan to seek three years marketing exclusivity in the U.S. if we receive FDA approval for Zelrix, we may not be entitled to such marketing exclusivity if the FDA determines that our clinical investigations were not essential to the approval of the Zelrix NDA. This three year marketing exclusivity period, if granted, would be coterminous with any patent coverage for Zelrix. We also intend to seek an additional period of six months pediatric exclusivity in the U.S., but may not be able to secure such exclusivity if the FDA does not request pediatric trials for Zelrix or we are unable to complete the trials that the FDA requests. The six month pediatric exclusivity period, if granted, would be in addition to the term of any existing regulatory exclusivity or listed patent term. If we are unable to secure marketing exclusivity and any patents that we are issued do not provide sufficient protection, our business and ability to generate revenues may be harmed significantly.

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.

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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;
- 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 products 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;

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The potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market, with low or 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.

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 March 31, 2010, we had an accumulated deficit of approximately $59.4 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 convertible preferred stock, 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 will incur 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.

Zelrix will require additional clinical trials and evaluation, 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.

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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:

- Complete development of and seek marketing approval for Zelrix;
- 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 expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to fund our operations and capital requirements for at least the next 24 months. We believe that these available funds will be sufficient to complete the development of Zelrix through FDA approval and to fund 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 significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control.

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

- The timing of our submission to the FDA and outcome of the FDA s review of the NDA for Zelrix;
- The extent to which the FDA may require us to perform additional clinical trials for Zelrix;
- The timing and success of this offering;
- The costs of our commercialization activities for Zelrix, if it is approved by the FDA;
- 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 cost, timing and outcome of regulatory review of our other product candidates;
- The extent to which we acquire or invest in products, businesses and technologies;
- The extent to which we choose to establish collaboration, co-promotion, distribution or other similar agreements for product candidates; and
- The costs of preparing, submitting and prosecuting patent applications and maintaining, enforcing and defending intellectual property claims.

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,

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making capital expenditures or declaring dividends. Any debt financing or additional equity that we raise may contain terms, such as liquidation and other preferences, that 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 recurring operating losses have raised substantial doubt regarding our ability to continue as a going concern.

Our recurring operating losses raise substantial doubt about our ability to continue as a going concern. As a result, our independent registered public accounting firm included an explanatory paragraph in its report on our financial statements as of and for the year ended December 31, 2009 with respect to this uncertainty. We have no current source of revenues to sustain our present activities, and we do not expect to generate revenues until, and unless, the FDA or other regulatory authorities approve Zelrix or our other product candidates and we successfully commercialize any such product candidates. Accordingly, our ability to continue as a going concern will require us to obtain additional financing to fund our operations. The perception of our ability to continue as a going concern may make it more difficult for us to obtain financing for the continuation of our operations and could result in the loss of confidence by investors, suppliers and employees.

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

Upon closing of this offering, we will have $5.0 million principal amount of indebtedness 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 Lohmann Therapie-Systeme AG, or 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.

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. Because of the covenants under our existing debt instruments and the pledge of our assets as collateral, we have a limited ability to obtain additional debt financing.

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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.

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 such 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 will be customized to the particular manufacturing specifications of Zelrix and does not exist currently. 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, or 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 to commercialize Zelrix or any other product candidates.

We currently rely on contract research organizations, or 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.

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, our development programs may be extended, delayed or terminated, and 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.

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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.

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, or 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;

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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 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.

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;

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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.

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;

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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, or 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. We intend to submit the proposed trade name Zelrix to the FDA for approval. If the FDA objects to our proposed trade name, 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 after we submit our NDA to the FDA and 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.

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;

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.

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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 are found to be not 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, or 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.

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.

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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.

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.

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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, or 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., or 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.

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.

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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.

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.

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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, which will be effective upon the closing of this offering, with Ms. Hollingsworth and Ms. Sebree and all of our other executive officers, that each include 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 June 30, 2010, we employed 22 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 this Offering and Ownership of Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the initial public offering price.

Prior to this offering, there has not been a public market for our common stock. If an active trading market for our common stock does not develop following this offering, you may not be able to sell your shares quickly or at the market price. The initial public offering price for the shares will be determined by negotiations between us and representatives of the underwriters and may not be indicative of prices that will prevail in the subsequent trading market.

The trading price of our common stock is likely to be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- Any delay in submitting our NDA for Zelrix and any adverse development or perceived adverse development with respect to the FDA s review of such NDA, 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;

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;

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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.

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.

Upon closing of this offering, our executive officers, directors and 5% stockholders and their affiliates will beneficially own approximately 52.30% of our outstanding voting stock. 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.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

The initial public offering price is substantially higher than the net tangible book value per share of our common stock. Investors purchasing common stock in this offering will pay a price per share that substantially exceeds the book value of our tangible assets after subtracting our liabilities. As a result, investors purchasing common stock in this offering will incur immediate dilution of $9.72 per share, assuming an initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus. Further, investors purchasing common stock in this offering will contribute approximately 56.0% of the total amount invested by stockholders since our inception, but will own only approximately 35.4% of the shares of our common stock outstanding.

This dilution is due to the substantially lower price paid by our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options granted to our employees. In addition, as of June 30, 2010, options to purchase 938,223 shares of our common stock at a weighted average exercise price of $1.81 per share and warrants exercisable for up to 1,126,298 shares of our preferred stock at an exercise price of $0.93 per share were outstanding. Moreover, as of the effective date of the registration statement for this offering, options to purchase an additional 345,350 shares of our common stock at an exercise price equal to the initial public offering price of $15.00 per share will be outstanding. The exercise of any of these options or warrants would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of a liquidation or sale of our company.

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Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise adequate capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

Substantially all of our existing stockholders are subject to lock-up agreements with the underwriters of this offering that restrict the stockholders ability to transfer shares of our common stock for at least 180 days from the date of this prospectus, subject to certain exceptions. The lock-up agreements limit the number of shares of common stock that may be sold immediately following the public offering. Subject to certain limitations, 9,110,653 shares will become eligible for sale upon expiration of the lock-up period. In addition, shares issued or issuable upon exercise of options and warrants vested as of the expiration of the lock-up period will be eligible for sale at that time. Sales of stock by these stockholders could have a material adverse effect on the market price of our common stock.

Certain holders of shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act of 1933, as amended, or the Securities Act, subject to the 180-day lock-up arrangement described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by our affiliates as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Our management will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and our stockholders will not have the opportunity as part of their investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing instruments and U.S. government securities. These investments may not yield a favorable return to our stockholders.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an ownership change, generally defined as a greater than 50% change by value in its equity ownership over a three year period, the corporation s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes, such as research tax credits, to offset its post-change income may be limited. We believe that, with our initial public offering, our most recent private placement and other transactions that have occurred over the past three years, we may have triggered an ownership change limitation. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we generate taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could result in increased future tax liability to us.

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.

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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 that will become effective following the closing of this offering, as well as provisions of the Delaware General Corporation Law, or 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:

Authorizing the issuance of blank check preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;

Prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;

Eliminating the ability of stockholders to call a special meeting of stockholders; and

Establishing advance notice requirements for nominations for election to the board of directors or 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.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words may, will, could, would, should, expect, intend, anticipate, believe, estimate, predict, project, potential, continue, ongoing and similar expressions are in identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus include, among other things, statements about:

- 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;
- Regulatory developments in the U.S. and foreign countries;
- The performance of third party manufacturers;
- Our ability to acquire or license suitable product candidates or technologies from third parties;
- The accuracy of our estimates regarding expenses and capital requirements; and
- The loss of key scientific or management personnel.

We may not actually achieve the plans, intentions or expectations described in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations described in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the Risk Factors section, that we believe could cause actual results or events to differ materially from those expressed or implied by our forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock. We do not assume any obligation to update any forward-looking statements.

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USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of 5,000,000 shares of common stock in this offering will be approximately $66.5 million, assuming an initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that our net proceeds from this offering will be approximately $76.9 million.

Each $1.00 increase or decrease in the assumed initial public offering price of $15.00 per share would increase or decrease the net proceeds to us from this offering by approximately $4.6 million, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We anticipate using the net proceeds from this offering as follows:

- Approximately $36.0 million to complete the clinical development of, seek marketing approval for, initiate the commercial manufacture of and, if approved, commercially launch Zelrix in the U.S.;

- Approximately $5.0 million to continue preclinical and clinical development of NP201 and NP202; and

- The balance for working capital and other general corporate purposes, which may include the acquisition or licensing of other products or technologies or the acquisition of other businesses in the biotechnology or specialty pharmaceuticals industry.

This anticipated use of net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including: the timing of our NDA submission to the FDA for Zelrix; the extent to which the FDA may require us to perform additional clinical trials for Zelrix; the costs of our commercialization activities for Zelrix, if it is approved by the FDA; the cost, timing and outcome of the development of our other product candidates; the extent to which we acquire or invest in products, businesses and technologies; the extent to which we establish collaboration or other similar agreements; the cost of preparing and prosecuting patent applications and enforcing and defending intellectual property claims; and any unforeseen or underestimated cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. In addition, our anticipated use of proceeds does not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make. We have no current understandings, agreements or commitments for any material acquisitions or licenses of any products, businesses or technologies.

Following this offering, we believe that our available funds will be sufficient to complete the development of Zelrix through FDA approval and to fund the expected commercial launch of Zelrix in the U.S. in the first half of 2012. It is possible that we will not achieve the progress that we expect with respect to Zelrix because the actual costs and timing of development and marketing approval are difficult to predict and are subject to substantial risks and delays. We have no committed external sources of funds. To the extent that the net proceeds from this offering and our other capital resources are insufficient to complete clinical development of, obtain marketing approval for and, if approved, commercially launch Zelrix, 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.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

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DIVIDEND POLICY

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. We do not intend to pay cash dividends on our common stock for the foreseeable future. In addition, the May 2010 Loan Facility restricts us from paying dividends on our capital stock. The terms of the May 2010 Loan Facility are described in more detail under Management s Discussion and Analysis of Financial Condition and Results of Operations Liquidity and Capital Resources Debt Facilities.

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CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of March 31, 2010:

On an actual basis;

On a pro forma basis to give effect to:

the automatic conversion of all outstanding shares of our preferred stock, including accrued dividends, into an aggregate of 7,858,934 shares of common stock upon the closing of this offering, assuming that the closing occurs on August 9, 2010;

the receipt in April 2010 of gross proceeds of $10,062,500 upon the issuance of the April 2010 Convertible Notes and the automatic conversion of all principal and accrued interest outstanding under the April 2010 Convertible Notes into an aggregate of 861,043 shares of common stock upon the closing this offering, assuming an initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and that the closing occurs on August 9, 2010;

the receipt in May 2010 of gross proceeds of $5,000,000 upon entering into the May 2010 Loan Facility, the issuance of warrants to purchase 255,376 shares of Series B preferred stock, with an estimated fair value of $203,255, to the lenders under such facility and the repayment in full of the $555,208 outstanding as of March 31, 2010 under a term loan that we entered into in 2007; and

the warrants outstanding as of June 30, 2010 to purchase an aggregate of 1,126,298 shares of our preferred stock becoming, in accordance with their terms, warrants to purchase 140,520 shares of common stock at an exercise price of $7.45 per share of common stock upon the closing of this offering and the reclassification of the warrant liability with respect to warrants outstanding as of March 31, 2010 to additional paid-in capital; and

On a pro forma as adjusted basis to give further effect to the issuance and sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma as adjusted information set forth below is illustrative only and our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table together with the Management s Discussion and Analysis of Financial Condition and Results of Operations section of this prospectus and our financial statements and the related notes appearing at the end of this prospectus.

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	As of March 31, 2010		
	Actual	Pro Forma	Pro Forma as Adjusted
	(Unaudited)		
	(In thousands, except share data)		
Cash and cash equivalents	$ 592	$ 15,100	$ 81,550
Debt outstanding	$ 564	$ 5,009	$ 5,009
Warrant liability	606		
Redeemable convertible preferred stock, $0.001 par value; 71,745,055 shares authorized and 53,096,340 shares issued and outstanding, actual; none, pro forma and pro forma as adjusted	56,572		
Stockholder s equity (deficit):			
Common stock, $0.001 par value; 28,254,945 shares authorized and 392,254 shares issued and outstanding, actual; 28,254,945 shares authorized and 9,112,231 shares issued and outstanding, pro forma; 90,000,000 shares authorized and 14,112,231 shares issued and outstanding, pro forma as adjusted		9	14
Additional paid-in capital		67,435	133,880
Deficit accumulated during the development stage	(59,390)	(59,391)	(59,391)
Total stockholders equity (deficit)	(59,390)	8,053	74,503
Total capitalization	$ (1,648)	$ 13,062	$ 79,512

Each $1.00 increase or decrease in the assumed initial public offering price of $15.00 per share would increase or decrease each of cash and cash equivalents, additional paid-in capital, total stockholders equity and total capitalization on a pro forma as adjusted basis by approximately $4.6 million, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The table above does not include:

938,223 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2010 at a weighted average exercise price of $1.81 per share;

345,350 shares of common stock issuable upon the exercise of options, to be granted effective upon the effective date of the registration statement for this offering, at an exercise price equal to the initial public offering price;

140,520 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2010 at a weighted average exercise price of $7.45 per share; and

791,776 additional shares of common stock reserved for future issuance under our 2010 Plan, which will become effective upon the effective date of the registration statement for this offering, including

105,555 shares of common stock reserved for issuance under our 2005 Plan, which shares will be added to the shares reserved for future issuance under our 2010 Plan upon effectiveness of our 2010 Plan.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of common stock and the pro forma net tangible book value per share of common stock after this offering.

Our historical net tangible book value of common stock as of March 31, 2010 was $(2.8) million, or $(7.19) per share of common stock. Historical net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by the total number of shares of common stock outstanding.

After giving effect, upon the closing of this offering, to the automatic conversion of all outstanding shares of our preferred stock, including accrued dividends, into an aggregate of 7,858,934 shares of common stock and the automatic conversion of all principal and accrued interest outstanding under the April 2010 Convertible Notes into an aggregate of 861,043 shares of common stock, assuming an initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and that the closing occurs on August 9, 2010, our pro forma net tangible book value as of March 31, 2010 would have been $8.1 million, or $0.88 per share of common stock.

After giving effect to our issuance and sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2010 would have been $74.5 million, or $5.28 per share of common stock. This represents an immediate increase in pro forma net tangible book value of $4.40 per share to our existing stockholders and an immediate dilution of $9.72 in pro forma net tangible book value per share to new investors purchasing shares of common stock in this offering.

Dilution per share to new investors purchasing shares of common stock in this offering is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share of common stock		$ 15.00
Historical net tangible book value per share as of March 31, 2010	$ (7.19)	
Increase in net tangible book value per share attributable to the conversion of outstanding preferred stock and April 2010 Convertible Notes	8.07	
Pro forma net tangible book value per share as of March 31, 2010	0.88	
Increase in net tangible book value per share attributable to new investors	4.40	
Pro forma as adjusted net tangible book value after this offering		5.28
Dilution per share to new investors		$ 9.72

Each $1.00 increase or decrease in the assumed initial public offering price of $15.00 per share would increase or decrease our pro forma as adjusted net tangible book value by approximately $4.6 million, our pro forma as adjusted net tangible book value per share by $0.33 and dilution per share to new investors purchasing shares of common stock

in this offering by $0.67, assuming that the number of shares of common stock offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their over-allotment option in full, the pro forma as adjusted net tangible book value per share after giving effect to this offering would be $5.71 per share and the dilution in pro forma as adjusted net tangible book value per share to new investors would be $9.29 per share.

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The following table summarizes, on a pro forma basis as described above as of March 31, 2010, the differences between the number of shares of common stock purchased from us, the total effective cash consideration paid and the average price per share paid by our existing stockholders and by new investors purchasing shares of common stock in this offering at an assumed initial public offering price of $15.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares Purchased		Total Consideration		Average Price per Share
	Number	Percent	Amount	Percent	
Existing stockholders	9,112,231	64.6%	$ 58,862,589	44.0%	$ 6.46
New investors	5,000,000	35.4	75,000,000	56.0	15.00
Total	14,112,231	100.0%	$ 133,862,589	100.0%	

Each $1.00 increase or decrease in the assumed initial public offering price of $15.00 per share would increase or decrease the total consideration paid by new investors by $4.6 million and increase or decrease the percentage of total consideration paid by new investors purchasing shares of common stock in this offering by approximately 1.6%, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same.

If the underwriters exercise their over-allotment option in full, our existing stockholders would own 61.3% and new investors would own 38.7% of the total number of shares of common stock outstanding after this offering.

The tables and calculations set forth above are based on the number of shares of common stock outstanding after the closing of this offering and assumes no exercise of any outstanding options or warrants. To the extent that options or warrants are exercised, there will be further dilution to new investors.

The above information excludes:

- 938,223 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2010 at a weighted average exercise price of $1.81 per share;
- 345,350 shares of common stock issuable upon the exercise of options, to be granted effective upon the effective date of the registration statement for this offering, at an exercise price equal to the initial public offering price;
- 140,520 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2010 at a weighted average exercise price of $7.45 per share; and
- 791,776 additional shares of common stock reserved for future issuance under our 2010 Plan, which will become effective upon the effective date of the registration statement for this offering, including 105,555 shares of common stock reserved for issuance under our 2005 Plan, which shares will be added to the shares reserved for future issuance under our 2010 Plan upon effectiveness of our 2010 Plan.

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SELECTED FINANCIAL DATA

You should read the following selected financial data together with the Capitalization and Management s Discussion and Analysis of Financial Condition and Results of Operations sections of this prospectus and our financial statements and the related notes appearing at the end of this prospectus. We have derived the statement of operations data for the years ended December 31, 2007, 2008 and 2009 and the balance sheet data as of December 31, 2008 and 2009 from our audited financial statements appearing at the end of this prospectus. We have derived the statement of operations data for the period from January 7, 2005 (inception) through December 31, 2005 and year ended December 31, 2006 and the balance sheet data as of December 2005, 2006 and 2007 from our audited financial statements not included in this prospectus. We have derived the statement of operations data for the three months ended March 31, 2009 and 2010 and the balance sheet data as of March 31, 2010 from our unaudited financial statements appearing at the end of this prospectus. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period and our interim period results are not necessarily indicative of results for a full year.

See note 3(j) to our financial statements appearing at the end of this prospectus for information regarding computation of basic and diluted net loss per common share, unaudited pro forma basic and diluted net loss per common share and the unaudited pro forma weighted average basic and diluted common shares outstanding used in computing pro forma basic and diluted net loss per common share.

	January 7, 2005 (inception) to December 31, 2005	Year Ended December 31, 2006	2007	2008	2009	Three Months Ended March 31, 2009	2010
						(Unaudited)	
	(In thousands, except share and per share data)						
Statement of Operations Data:							
Operating expenses:							
Research and development	$ 692	$ 3,209	$ 7,761	$ 8,815	$ 11,310	$ 2,996	$ 3,390
Acquired in-process research and development				5,500			
General and administrative	364	1,363	1,884	3,075	3,142	796	873
Total operating expenses	(1,056)	(4,572)	(9,645)	(17,390)	(14,452)	(3,792)	(4,263)
Interest income (expense), net	(12)	(644)	(30)	(121)	(1,289)	(37)	(10)
Loss before tax benefit	(1,068)	(5,216)	(9,675)	(17,511)	(15,741)	(3,829)	(4,273)

Income tax benefit					151	151	320
Net loss	(1,068)	(5,216)	(9,675)	(17,511)	(15,590)	(3,678)	(3,953)
Accretion of redeemable convertible preferred stock		(341)	(1,126)	(2,330)	(3,617)	(830)	(1,033)
Net loss applicable to common stockholders	$ (1,068)	$ (5,557)	$ (10,801)	$ (19,841)	$ (19,207)	$ (4,508)	$ (4,986)
Basic and diluted net loss per common share	$ (3.50)	$ (16.25)	$ (29.38)	$ (51.98)	$ (50.31)	$ (11.81)	$ (13.06)
Weighted average basic and diluted common shares outstanding	305,100	341,979	367,691	381,681	381,789	381,789	381,842
Unaudited pro forma net loss					$ (15,590)		$ (3,953)
Unaudited pro forma basic and diluted net loss per common share					$ (2.04)		$ (0.45)
Unaudited pro forma weighted average basic and diluted common shares outstanding					7,654,193		8,823,612

	As of December 31,					As of March 31,
	2005	2006	2007	2008	2009	2010 (Unaudited)
	(In thousands)					
Balance Sheet Data:						
Cash and cash equivalents	$ 1,003	$ 5,211	$ 3,830	$ 8,368	$ 3,927	$ 592
Working capital	652	4,347	1,304	6,285	1,527	(2,372)
Total assets	1,109	5,400	4,462	9,776	5,009	1,580
Long-term debt	1,600		1,628	782		
Redeemable convertible preferred stock		10,164	16,270	41,809	55,538	56,572
Total stockholders deficit	(851)	(5,716)	(16,458)	(36,141)	(54,474)	(59,390)

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MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing at the end of prospectus. In addition to historical information, some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated or implied in these forward-looking statements as a result of important factors described in the cautionary statements included in this prospectus, particularly in the Risk Factors section.

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 successfully completed a pivotal Phase III clinical trial for Zelrix in July 2009 and expect to submit an NDA to the FDA in the fourth quarter of 2010. Before we submit our NDA, we must complete two ongoing pharmacokinetic trials in healthy subjects and obtain interim data from two Phase III safety trials. 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 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 revenue and have never been profitable. Our net loss was $4.0 million in the three months ended March 31, 2010, $15.6 million for the year ended December 31, 2009 and $17.5 million for the year ended December 31, 2008. As of March 31, 2010, we had an accumulated deficit of $59.4 million.

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 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, including personnel to support our planned product commercialization efforts. We also expect to incur significant costs to comply with corporate governance, internal controls and similar requirements applicable to us as a public company following the closing of this offering. Our results may vary depending on many factors, including the progress and results of our preclinical studies and clinical trials, our ability to obtain marketing approval of Zelrix and our other product candidates and, if approved, our ability to commercialize these products and achieve market acceptance of these products among physicians, patients and third party payors.

We have funded our operations to date primarily with the proceeds of the sale of convertible preferred stock, convertible notes and borrowings under debt facilities. From inception through March 31, 2010, we have received net proceeds of $48.0 million from the sale of convertible preferred stock and convertible notes. As of March 31, 2010,

we had $0.6 million of debt outstanding under a term loan that we entered into in 2007.

In April 2010, we received gross proceeds of $10.1 million from the sale of the April 2010 Convertible Notes. Further, in May 2010, we entered into the May 2010 Loan Facility under which $5.0 million was advanced on the closing date. We used a portion of the proceeds that we received on the closing date of the

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May 2010 Loan Facility to repay all outstanding amounts under the term loan that we entered into in 2007. The April 2010 Convertible Notes and the May 2010 Loan Facility are described in more detail under Liquidity and Capital Resources.

Our recurring losses and negative cash flows from operations raise substantial doubt about our ability to continue as a going concern. As a result, our independent registered public accounting firm included an explanatory paragraph regarding this uncertainty in its report on our financial statements as of and for the year ended December 31, 2009. We have no current source of revenues to sustain our present activities, and we do not expect to generate revenues until, and unless, the FDA or other regulatory agencies approve Zelrix or any other of our product candidates and we successfully commercialize any such product candidates. Accordingly, our ability to continue as a going concern will require us to obtain additional financing to fund our operations.

Financial Overview

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, contractor 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, contractor 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 March 31, 2010, we incurred research and development expenses of $35.2 million, of which $24.9 million related to the development of Zelrix. We incurred research and development expenses associated with the development of Zelrix of $2.5 million in the three months ended March 31, 2010, $8.2 million in 2009 and $5.6 million in 2008. Additionally, in 2008 we incurred $5.5 million of acquired in-process

research and development expenses in connection with our acquisition of a patent application utilized in Zelrix. In addition, pursuant to this transaction, we obtained a perpetual, worldwide, exclusive, royalty-free license, with the right to grant sublicenses, including issued U.S. Patent No. 6,745,071, as described in more detail under Business Intellectual Property and Exclusivity. Salaries and related expenses included in research and development expenses were $0.7 million in the three months

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ended March 31, 2010, $2.4 million in 2009 and $6.7 million since our inception. We do not allocate salaries and related expenses to individual projects, trials or studies or to specific product candidates.

We expect that our research and development expenses in 2010 will be higher than in 2009 as a result of the full enrollment of the Phase III safety trials for Zelrix and the increased regulatory work related to the NDA that we expect to submit for Zelrix during the fourth quarter of 2010. We also expect to incur additional research and development expenses in 2010 as we accelerate the development of NP201 and NP202. These expenditures are subject to numerous uncertainties regarding timing and cost to completion. Completion of our preclinical development and clinical trials may take several years or more and the length of time generally varies according to the type, complexity, novelty and intended use of a product candidate. The cost of clinical trials may vary significantly over the life of a project as a result of differences arising during clinical development, including, among others:

The number of sites included in the trials;

The length of time required to enroll suitable subjects;

The size of subject populations participating in the trials;

The duration of subject follow-ups;

The development stage of the product candidates; and

The efficacy and safety profile of the product candidates.

Neither Zelrix nor any of our other product candidates has received FDA approval. In order for the FDA to approve a product candidate, the FDA must conclude that clinical data establishes the safety and efficacy of such product candidate. We currently anticipate submitting an NDA for Zelrix in the fourth quarter of 2010. We expect to incur research and development costs of approximately $11 million to $13 million through the end of 2011 to complete development of Zelrix. As discussed above, due to the numerous risks and uncertainties associated with timing and costs to completion of clinical trials, we cannot determine these future expenses with certainty and the actual range may vary significantly from our forecast.

Additionally, we expect to incur aggregate costs of approximately 5.4 million relating to the funding of commercial manufacturing equipment for Zelrix, as described in more detail under Business License, Development and Commercial Agreements LTS Lohmann Therapie Systeme AG. As of June 30, 2010, 3.8 million, or approximately $4.7 million based on exchange rates in effect as of June 30, 2010, remain to be paid in monthly installments under this agreement. 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 NP202 in 2012. Due to their early stages of development, we are unable to determine the duration and completion costs of our NP201 and NP202 development projects. As a result of the difficulties forecasting NP201 and NP202 development costs, as well as the other uncertainties discussed above, we are unable to determine when and to what extent we will generate revenues from the commercialization and sale of an approved product candidate.

General and Administrative Expenses

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 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, consulting, tax and accounting services, insurance, depreciation and general corporate expenses. We expect that our general and administrative expenses will increase with the continued development and potential commercialization of our product candidates.

We expect that our general and administrative expenses in 2010 will be higher than in 2009 as a result of greater expenses relating to our operations 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. Additionally, we plan to increase spending related to building a commercial infrastructure for the anticipated launch of Zelrix in the U.S. in the first half of 2012. However, in an effort to control our spending related to commercialization efforts, we currently plan to hire most of our sales and marketing personnel only if Zelrix is approved by the FDA.

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. Excluding the impact of non-cash interest costs, we expect interest expense to increase in 2010 compared with 2009 as a result of the April 2010 Convertible Notes and the May 2010 Loan Facility.

Net Operating Losses and Tax Loss Carryforwards

Our net loss was $4.0 million for the three months ended March 31, 2010 and $15.6 million for the year ended December 31, 2009. We have incurred cumulative net losses of $53.0 million from inception through March 31, 2010. As of December 31, 2009, we had approximately $43.4 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 2024. 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, 2009.

The closing of this offering, 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, which could result in increased future tax liability to us.

Critical Accounting Policies and Use of Estimates

We have based our management s discussion and analysis of our financial condition and results of operations on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. The preparation of these financial statements 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 appearing at the end of this prospectus, 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 and stock price volatility. As a private 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 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. 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. The risk-free interest rate is based on U.S. Treasury instruments with a remaining term equal to the expected term of the option. 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.

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 represents 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.

Prior to December 2006, our board of directors or our compensation committee estimated the fair value of our common stock considering the following factors:

- The nature and history of our business;
- The general economic outlook and the outlook for the life sciences industry;
- Our financial condition and results of operations, including important developments in our operations, most significantly relating to the clinical development of our most advanced product candidate, Zelrix;
- Our ability to pay dividends;
- Whether or not we had goodwill or other intangible value;
- Our past transactions in common stock and preferred stock; and
- The stock prices of other publicly traded companies engaged in lines of business that are the same or similar to ours.

Beginning in December 2006, our compensation committee obtained independent third party valuations to assist it in estimating the fair value of our common stock. These valuations took into account clinical and other notable

milestones with respect to Zelrix. The first independent third party valuation of our common stock took place following the sale of Series A preferred stock in August 2006 when we engaged an independent third party valuation firm to assist our compensation committee in determining the fair value of our common stock as of December 31, 2006. In connection with the sale of Series B preferred stock in July 2008, and in anticipation of the grant of a significant number of stock options covering our common stock in the third quarter of 2008, we again engaged an independent third party valuation firm to assist our compensation committee in determining the fair value of our common stock as of July 8, 2008.

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The following table summarizes the proceeds from the issuance of our preferred stock through June 30, 2010:

Issuance	Date	Number of Shares	Net Proceeds (In millions)
Series A preferred stock	August and October 2006	11,546,161	$ 9.7
Series A preferred stock	October 2007	5,376,345	5.0
Series B preferred stock	April and July 2008	25,282,556	23.2
Series B preferred stock	August 2009	10,891,278	10.1
		53,096,340	$ 48.0

Although we sold all of the shares of Series A and Series B preferred stock at a price of $0.93 per share, our compensation committee did not believe that the value placed on these shares of preferred stock provided a direct indication of the fair value of our common stock because the preferred stock is entitled to preferences, rights and protections that are not applicable to our common stock. As of June 30, 2010, because of these preferences, the holders of the Series A and Series B preferred stock were entitled to receive a liquidation preference of $57.8 million and to participate with the common stockholders on an as-converted basis in the remaining value of our company.

In order to estimate the fair value of our common stock, we estimated the aggregate fair value of our common stock and preferred stock, which we refer to as our aggregate equity value, and then allocated this value between our preferred stock and common stock using a Black-Scholes call option method, as described in more detail below. In addition, we applied an illiquidity discount to our estimate of the fair value of our common stock to account for the heightened level of risk of our shares compared to shares of comparable, publicly traded companies.

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.

Under the market-based approach, we calculated the valuation multiples relative to the total assets, equity and cash-on-hand for comparable, publicly traded companies. We then applied those multiples to our assets, equity and cash-on-hand as of the valuation date.

We considered comparable companies to be publicly traded companies that have pharmaceutical and biopharmaceutical product candidates in the early stages of development or clinical trials that could be considered comparable to us for valuation purposes. We primarily considered public companies that had a limited group of drug or product candidates that were in comparable stages of clinical development.

For purposes of the December 31, 2006 valuation, we searched for publicly traded companies that had drug or product candidates that were in Phase I clinical trials or preclinical development with up to $15.0 million in revenues. Additionally, we reviewed information regarding potential competitors and researched companies that we historically have used as benchmarks for financial or operational comparison purposes. In order to determine the most comparable companies, we reviewed the business descriptions, product candidates and financial characteristics of these companies. Some of the companies had product candidates targeting similar markets as our product candidates. From this group of companies, we selected the most

comparable entities for valuation purposes.

For purposes of the July 8, 2008 valuation, our search for comparable publicly traded companies was consistent in the approach for the December 31, 2006 valuation, except that we primarily searched for publicly traded companies that had a drug or product candidates that were in the early stages of a Phase III clinical trial or that had drug or product candidates in Phase I or Phase II clinical development with up to $15.0 million in revenues.

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Under the asset-based approach, we calculated the fair value of our assets based on an estimate of how much it might cost a third party to replace or replicate our assets. This approach is based on the concept that a prudent investor would pay no more for an asset than the amount it would cost the investor to replace the asset with a new asset. In addition, this method assumes that a buyer of our company would be willing to pay us for the cost that the buyer would incur to replicate our investment in our product candidates. Accordingly, under this method, we estimated our aggregate equity value as the sum of the market value of our net tangible assets and the cumulative research and development cost that we incurred on Zelrix and our other product candidates through the valuation date.

The aggregate equity values for the market and asset-based approaches were similar. However, we ultimately derived the aggregate equity value in our December 31, 2006 and July 8, 2008 valuations from the market-based approach. We then allocated the aggregate equity value between the common stock and the preferred stock using a Black-Scholes call option pricing method. Under this method, we estimated the fair value of our common stock as the net value of a series of call options, representing the present value of the expected future returns to the common stockholders. We considered the rights of the common stockholders to be equivalent to a call option on our future value in excess of the aggregate liquidation preferences payable on Series A and Series B preferred stock, with adjustments to account for the rights retained by the preferred stockholders related to any value in excess of the applicable liquidation preferences. Using this method, we valued the common stock by estimating the value of a share of common stock in each of these call option rights.

As discussed above, we then reduced the value of the common stock using this approach by applying an illiquidity discount to account for the heightened level of risk associated with our shares compared to that of comparable, publicly traded companies.

The December 31, 2006 valuation of our common stock was based on an aggregate equity value of $8.5 million. The value allocated to the common stock after applying the call option allocation methodology and a 35% illiquidity discount was $1.44 per share. Our compensation committee believed the increase in the estimated fair value of common stock from $0.96 per share prior to December 2006 to $1.44 per share was appropriate in light of the continued progress of Zelrix in its preclinical development program as of December 2006, coupled with the initial sale of Series A preferred stock in August 2006 at $0.93 per share.

The July 8, 2008 valuation of our common stock was based on an aggregate equity value of $30.2 million. The value allocated to the common stock after applying the call option allocation methodology and a 35% illiquidity discount was $1.92 per share. The increase in the aggregate equity value compared to the December 31, 2006 valuation reflected our sale of additional Series A preferred stock in October 2007, the initial sale of Series B preferred stock in July 2008 and the continued investment in, and advancement of, our product candidates. In particular, in the first quarter of 2008, we successfully completed a Phase I proof of concept study for Zelrix that provided encouraging pharmacokinetic data that was a predicate for continued development.

On each grant date subsequent to December 31, 2006, our compensation committee considered the most current independent valuation that had been completed and the continued validity of that valuation given the progress, if any, that we had made in the development of Zelrix and our other product candidates, external market factors and other conditions, as discussed above. The following table summarizes our stock-based awards issued since our inception to December 31, 2009. We have not issued any stock-based awards since December 31, 2009.

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Issuance Date	Per Share Fair Value of Preferred Stock on a Common Stock Equivalent Basis[1]	Per Share Fair Value of Common Stock[2]	Number of Awards: Common Stock	Number of Awards: Options[3]	Number of Awards: Total
1/1/2005 - 6/30/2005		$ 0.64	13,723		13,723
7/1/2005 - 12/31/2005		0.80		34,646	34,646
1/1/2006 - 6/30/2006		0.96	52,405[4]	16,217	68,622
7/1/2006 - 12/31/2006	$ 7.45	1.44	61,753[4]	46,890	108,643
1/1/2007 - 6/30/2007	7.45	1.44		21,207	21,207
7/1/2007 - 12/31/2007	7.45	1.44		47,094	47,094
1/1/2008 - 6/30/2008	7.45	1.44		14,346	14,346
7/1/2008 - 12/31/2008	7.45	1.92		734,816	734,816
1/1/2009 - 6/30/2009	7.45	1.92		57,970	57,970
7/1/2009 - 12/31/2009	7.45	1.92		10,477	10,477
			127,881	983,663	1,111,544

(1) Reflects the fair value of the preferred stock on a per share basis after giving effect to the ratio at which the preferred stock will convert into common stock based on the reverse split of our common stock that was effected on July 20, 2010.

(2) The per share estimated fair value of our common stock as determined by our compensation committee as of the date of the grant, taking into account various factors and including the results, if applicable, of independent third party valuations of our common stock as discussed above.

(3) All options were granted with an exercise price equal to the then fair value of our common stock.

(4) Represents restricted common stock awards subject to vesting criteria.

On July 14, 2010, we and the underwriters determined the estimated price range for this offering, as set forth on the cover page of this prospectus. The midpoint of the price range is $15.00 per share. In comparison, our estimate of the fair value of our common stock was $1.92 per share as of July 8, 2008. This estimate of fair value as of July 8, 2008 was based on an independent third party valuation report received by us. We note that, as we believe is typical in initial public offerings, the price range for this offering was not derived using a formal determination of fair value. Rather, it was determined based upon discussions between us and the underwriters. Among the factors that were considered in setting this range were prevailing market conditions and the prospects for our company and the industry in which we operate. Specifically, we believe that the increase in the fair value of our common stock since July 8, 2008 is primarily the result of the following factors:

The continued development of Zelrix since July 2008, including:

the initiation and subsequent successful completion of a pivotal Phase III clinical trial in July 2009;

the completion of enrollment of patients and, through June 30, 2010, treatment of over 6,250 migraines in two Phase III safety trials;

the commencement of two additional pharmacokinetic trials, which were initiated in December 2009 and February 2010;

the July 2010 notification by the FDA that the skin sensitization data being collected during our two Phase III safety trials has the potential to be sufficient, subject to review by the FDA as part of the NDA for Zelrix, without the need to conduct a separate skin sensitization study;

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our execution of the equipment funding agreement with LTS on June 1, 2010, whereby LTS began the purchasing, development and construction of the equipment necessary to produce our commercial supply of Zelrix; and

our recent determination that we believe we will submit an NDA for Zelrix in the fourth quarter of 2010.

The advancement of our NP201 product candidate since July 2008, including:

the completion of a proof of concept study in a well-accepted animal model for Parkinson s disease;

our execution of a license agreement with SurModics, on September 23, 2009, whereby we received an exclusive worldwide license to certain of Surmodics intellectual property;

the completion of a pre-IND meeting with the FDA in the first quarter of 2010; and

our recent determination that we believe we will submit an IND for NP201 in the first half of 2011.

The advancement of our NP202 product candidate since July 2008, including:

the commencement of the development of prototype products for NP202;

the commencement of pre-IND activities for NP202; and

our recent determination that we believe we will submit an IND for NP202 in 2012.

We believe that when the independent third party valuation was performed in July 2008, general market conditions (both private and public) were extremely negative. We believe that the markets have demonstrated a significant improvement. Notably, the AMEX Biotechnology Index has increased by approximately 36% from July 8, 2008 through July 14, 2010.

We also believe that it is reasonable to expect that the completion of this offering will result in increased liquidity and stockholders ability to sell shares of our common stock in the public markets. In addition, upon the closing of this offering, the preferred stock currently outstanding will automatically convert into shares of common stock and, as a result, the common stock will not be subject to any preferred preferences, rights or protections upon closing.

Results of Operations

Comparison of Three Months Ended March 31, 2009 and 2010

Research and Development Expenses

Research and development expenses for the three months ended March 31, 2009 and 2010 were comprised of the following:

	Three Months Ended March 31,	Increase (Decrease)

	2009	2010	$	%
	(In thousands)			
Clinical development, regulatory and manufacturing expenses	$ 1,774	$ 2,499	$ 725	41%
Research and preclinical expenses	503	114	(389)	(77)
Compensation and related expenses	599	673	74	12
Facilities and related expenses	120	104	(16)	(13)
	$ 2,996	$ 3,390	$ 394	13

Research and development expenses increased by $0.4 million, or 13%, to $3.4 million in the three months ended March 31, 2010 from $3.0 million in the three months ended March 31, 2009. This increase resulted primarily from a $0.3 million increase in manufacturing costs related to production of Phase III clinical supplies of Zelrix and a $0.4 million increase due to our continued Phase III clinical program for Zelrix, offset by a $0.4 million decrease in preclinical expenses, reflecting the completion in 2009 of a

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substantial portion of our preclinical studies for Zelrix and our increased focus on our Phase III clinical program for Zelrix. Research and development headcount remained consistent for the three months ended March 31, 2009 as compared to the three months ended March 31, 2010, with the minimal increase in compensation and related expenses resulting from annual increases in salary, bonus and benefit premiums.

Research and development expenses by program for the three months ended March 31, 2009 and 2010 are presented below:

	Three Months Ended March 31,		Increase (Decrease)	
	2009	2010	$	%
	(In thousands)			
Zelrix	$ 2,206	$ 2,542	$ 336	15%
NP201	70	70		
Development expenses general	720	778	58	8
	$ 2,996	$ 3,390	$ 394	13

The increase in spending on Zelrix in the three months ended March 31, 2010 was primarily due to the continuation of our Phase III clinical program and the related manufacture of Phase III clinical supplies, offset by lower preclinical spending due to the completion of many of our preclinical studies in 2009. Spending on NP201 remained consistent for the three months ended March 31, 2009 as compared to the three months ended March 31, 2010. The spending in the first quarter of 2009 was for NP201 preclinical studies and the spending in the first quarter of 2010 was for consulting expenses for NP201. 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.

General and Administrative Expenses

General and administrative expenses increased to $0.9 million in the three months ended March 31, 2010 from $0.8 million for the three months ended March 31, 2009. This increase resulted primarily from a $42,000 increase in marketing expenses due to higher consulting fees and a $30,000 increase in compensation expenses due to annual merit salary increases.

Interest Income/Expense

Interest income decreased to $1,000 in the three months ended March 31, 2010 from $19,000 in the three months ended March 31, 2009 due to lower average cash and cash equivalent balances.

Interest expense decreased to $11,000 in the three months ended March 31, 2010 from $56,000 in the three months ended March 31, 2009 primarily as a result of lower outstanding amounts due under the term loan we entered into in 2007. In addition, interest expense decreased by $20,000 due to the impact of a favorable non-cash adjustment for the mark-to-market of outstanding warrant liabilities as of March 31, 2010.

Income Tax Benefit

We recognized an income tax benefit of $320,000 in the three months ended March 31, 2010 and $151,000 in the three months ended March 31, 2009 related to the sale of Pennsylvania research and development tax credits to a third party buyer.

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Comparison of Years Ended December 31, 2008 and 2009

Research and Development Expenses

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

	Year Ended December 31,		Increase (Decrease)	
	2008	2009	$	%
	(In thousands)			
Clinical development, regulatory and manufacturing expenses	$ 4,257	$ 7,081	$ 2,824	66%
Research and preclinical expenses	2,172	1,385	(787)	(36)
Compensation and related expenses	1,950	2,388	438	22
Facilities and related expenses	436	456	20	5
	$ 8,815	$ 11,310	$ 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 costs related to our pivotal Phase III clinical trial and our Phase III safety trials for Zelrix and a $0.4 million increase in compensation costs, offset by a $0.6 million decrease in preclinical expenses, reflecting our focus on our Phase III clinical program for Zelrix, and a $0.6 million decrease in manufacturing expenses. The increase in compensation 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 our 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, 2008 and 2009 are presented below:

	Year Ended December 31,		Increase (Decrease)	
	2008	2009	$	%
	(In thousands)			
Zelrix	$ 5,590	$ 8,183	$ 2,593	46%
NP201	743	244	(499)	(67)
Development expenses general	2,482	2,883	401	16
	$ 8,815	$ 11,310	$ 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, directed 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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General and Administrative Expenses

General and administrative expenses were $3.1 million in both 2009 and 2008. Although 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.

Comparison of Years Ended December 31, 2007 and 2008

Research and Development Expenses

Research and development expenses for the years ended December 31, 2007 and 2008 were comprised of the following:

	Year Ended December 31,		Increase (Decrease)	
	2007	2008	$	%
	(In thousands)			
Clinical development, regulatory and manufacturing expenses	$ 5,063	$ 4,257	$ (806)	(16)%
Research and preclinical expenses	1,347	2,172	825	61
Compensation and related expenses	1,098	1,950	852	78
Facilities and related expenses	253	436	183	72
	$ 7,761	$ 8,815	$ 1,054	14

Research and development expenses increased by $1.1 million, or 14%, to $8.8 million in 2008 from $7.8 million in 2007. This increase resulted primarily from a $0.7 million increase in preclinical expenses related to toxicology studies for Zelrix and preclinical studies for NP201 that were initiated in 2008, a $0.9 million increase in compensation costs and a $0.2 million increase in facilities and related expenses, offset by a $0.6 million decrease in manufacturing expenses and a $0.2 million decrease in regulatory costs due to the submission of our IND for Zelrix in

2007. The increase in compensation costs in 2008 primarily reflected our addition of research and development personnel, particularly in the areas of quality assurance, regulatory and medical, throughout 2008. The increase in facilities and related expenses in 2008 resulted from the leasing of our new corporate headquarters in Conshohocken, Pennsylvania in March 2008. The decrease in manufacturing expenses in 2008 primarily reflected our substantial completion of the formulation and test method development for Zelrix in 2007.

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Research and development expenses by program for the years ended December 31, 2007 and 2008 are presented below:

	Year Ended December 31,		Increase (Decrease)	
	2007	2008	$	%
	(In thousands)			
Zelrix	$ 5,837	$ 5,590	$ (247)	(4)%
NP201	559	743	184	33
Development expenses general	1,365	2,482	1,117	82
	$ 7,761	$ 8,815	$ 1,054	14

The decrease in spending on Zelrix in 2008 is described in more detail above. The increase in spending on NP201 in 2008 specifically related to a preclinical study that we initiated in 2008. As also described above, our increased research and development headcount in 2008 was the primary reason for the increase in general research and development expenses in 2008.

General and Administrative Expenses

General and administrative expenses increased by $1.2 million, or 63%, to $3.1 million in 2008 from $1.9 million in 2007. This increase resulted primarily from a $0.5 million increase in compensation expenses associated with additional headcount, a $0.2 million increase in market research expenses, a $0.2 million increase in legal expenses and a $0.3 million increase in facility related expenses due to the leasing of our new corporate headquarters in March 2008.

Interest Income/Expense

Interest income decreased to $158,000 in 2008 from $223,000 in 2007 due to lower average cash and cash equivalent balances and lower yields on investments.

Interest expense increased to $278,000 in 2008 from $253,000 in 2007 due to a full year of expense related to a term loan entered into in March 2007 for $2.5 million.

Liquidity and Capital Resources

Since our inception in 2005, we have devoted most of our cash resources to research and development and general and administrative activities primarily related to the development of Zelrix. We have financed our operations primarily with the proceeds of the sale of convertible preferred stock and convertible notes and borrowings under debt facilities. To date, we have not generated any revenues from the sale of products, and we do not anticipate generating any revenues from the sale of Zelrix until at least 2012. We have incurred losses and generated negative cash flows from operations since inception. As of March 31, 2010, our principal sources of liquidity were our cash and cash equivalents, which totaled $0.6 million. Our working capital was $(2.4) million as of March 31, 2010.

Equity Financings

From inception through March 31, 2010, we have received net proceeds of $48.0 million from the sale of convertible preferred stock and convertible notes. The various issuances of our preferred stock are described in more detail under Critical Accounting Policies and Use of Estimates Stock-Based Compensation.

Debt Facilities

As of March 31, 2010, we had $0.6 million of debt outstanding under a term loan that we entered into in 2007. In April 2010, we received gross proceeds of $10.1 million from the sale of the April 2010 Convertible Notes. These notes bear interest at 8% per year and are due on December 31, 2010, if not converted prior to such date. The outstanding principal balance and accrued interest on the April 2010 Convertible Notes will

convert into shares of common stock upon the closing of this offering at a conversion price equal to 80% of the price to the public in this offering.

In May 2010, we entered into the May 2010 Loan Facility to fund our working capital requirements. Under the May 2010 Loan Facility, $5.0 million was advanced on the closing date, which we refer to as the Term A Loan, and, upon our receipt of at least $30.0 million in unrestricted net cash proceeds from the sale of equity securities, including pursuant to this offering, the private sale of equity or convertible debt securities, or upfront payments from a joint venture or partnership, we will have a 12-month period during which we may request an additional $6.0 million in funding, which we refer to as the Term B Loan. We refer to the Term A and Term B Loans together as the Term Loans. The funding of the Term B Loan is 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. The Term Loans have a scheduled maturity date in August 2013. The May 2010 Loan Facility 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.

We used $0.4 million of the proceeds from the Term A Loan to repay all outstanding amounts owed under the term loan that we entered into in 2007. Amounts outstanding under the May 2010 Loan Facility bear interest at LIBOR plus 8.75% per year, with a LIBOR floor of 3%. Until June 2011, the Term Loans only require monthly payments of interest. Thereafter, the Term Loans will amortize on a straight line basis, and we will be required to pay 27 equal monthly installments of principal and interest through the maturity date.

The May 2010 Loan Facility does not contain any financial covenants, although it does contain operating covenants, including covenants restricting our ability to incur additional indebtedness, pay dividends or other distributions, effect a sale of any part of our business and merge with or acquire another company. The May 2010 Loan Facility also includes customary events of default, including upon the occurrence of a payment default, a covenant default, a material adverse change and our insolvency. Further, the May 2010 Loan Facility provides for a three day cure period for a breach of payment obligations other than payment of principal and interest, for which no cure period is provided. A ten day cure period, which may be extended to up to 30 days in certain circumstances, is also provided for defaults that do not constitute an event of default under the May 2010 Loan Facility, breach specified affirmative covenants or breach a negative covenant.

In connection with the Term A Loan, we issued the lenders warrants to purchase 255,376 shares of Series B preferred stock at an exercise price of $0.93 per share. The number of shares exercisable under the warrant will automatically increase by up to an additional 306,452 shares of Series B preferred stock if the Term B Loan is funded in full. The warrants have a ten year exercise period and include a put option right in favor of the lenders in connection with certain major corporate events, events of default and maturity of the May 2010 Loan Facility. Upon the closing of this offering, in accordance with their terms, the put option right will terminate and the outstanding warrants will automatically become exercisable for 31,861 shares of common stock at an exercise price of $7.45 per share of common stock.

Future Capital Requirements

We expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to fund our operations and capital requirements, including payment obligations under our outstanding debt, for at least the next 24 months. We believe that these available funds will be sufficient to complete the development of Zelrix through FDA approval and to fund the expected commercial launch of Zelrix in the U.S. in the first half of 2012. However, it is difficult to predict our spending relative to Zelrix and our other product candidates prior to obtaining FDA approval. Moreover, changing circumstances may cause us to expend cash significantly faster than we currently anticipate, and we may need to spend more cash than currently expected because of circumstances beyond our control.

Our expectations regarding future cash requirements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we make in the future. We have no current understandings, agreements or commitments for any material acquisitions or licenses of any products,

businesses or technologies. We may need to raise substantial additional capital in order to engage in any of these types of transactions.

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 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, including personnel to support our planned product commercialization efforts. We also expect to incur significant costs to comply with corporate governance, internal controls and similar requirements applicable to us as a public company following the closing of this offering.

Our future use of operating cash and capital requirements will depend on many forward-looking factors, including the following:

- The timing of our submission to the FDA, and outcome of the FDA s review, of the NDA for Zelrix;
- The extent to which the FDA may require us to perform additional clinical trials for Zelrix;
- The timing and success of this offering;
- The costs of our commercialization activities for Zelrix, if it is approved by the FDA;
- 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 cost, timing and outcome of regulatory review of our other product candidates;
- The extent to which we acquire or invest in products, businesses and technologies;
- The extent to which we choose to establish collaboration, co-promotion, distribution or other similar agreements for product candidates; and
- The costs of preparing, submitting and prosecuting patent applications and maintaining, enforcing and defending intellectual property claims.

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 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, that 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.

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Cash Flows

The following table summarizes our cash flows from operating, investing and financing activities for the years ended December 31, 2007, 2008 and 2009 and the three months ended March 31, 2009 and March 31, 2010:

	Year Ended December 31,			Three Months Ended March 31,	
	2007	2008	2009	2009	2010
			(In thousands)		
Statement of Cash Flows Data:					
Total cash provided by (used in):					
Operating activities	$ (8,629)	$ (12,274)	$ (13,568)	$ (2,844)	$ (3,063)
Investing activities	(36)	(5,627)	(29)	(12)	(20)
Financing activities	7,284	22,439	9,155	(236)	(251)
Increase (decrease) in cash and cash equivalents	$ (1,381)	$ 4,538	$ (4,442)	$ (3,092)	$ (3,334)

Operating Activities

Net cash used in operating activities for the three months ended March 31, 2010 was $3.1 million, an increase of $0.2 million from the three months ended March 31, 2009. This increase was due to increased spending on our Phase III clinical program for Zelrix, which was in a more advanced stage in the three months ended March 31, 2010 than in the three months ended March 31, 2009.

Net cash used in operating activities for the year ended December 31, 2009 was $13.6 million, an increase of $1.3 million from the year ended December 31, 2008. This increase was primarily due to a $3.2 million increase in research and development expenses for our pivotal Phase III clinical trial and our Phase III safety trials for Zelrix, partially offset by a $0.6 million decrease in manufacturing expenses and a $0.6 million decrease in preclinical development expenses, as described in more detail under Results of Operations. Net cash used in operating activities for the year ended December 31, 2008 was $12.3 million, an increase of $3.6 million from the year ended December 31, 2007. This increase was primarily due to the $2.2 million increase in operating expenses in 2008, as described in more detail under Results of Operations, and $0.7 million for prepaid clinical supplies that we purchased in 2008 for use in future clinical trials.

We expect cash used in operating activities to increase in 2010 as compared to 2009 due to an expected increase in our operating losses associated with the Phase III safety trials for Zelrix and costs associated with the expected submission of an NDA for Zelrix during the fourth quarter of 2010 and the expected acceleration of our preclinical development programs.

Investing Activities

Cash used in investing activities for the purchase of property and equipment was $12,000 in the three months ended March 31, 2009 and $20,000 in the three months ended March 31, 2010.

Cash used in investing activities for the purchase of property and equipment was $29,000 in 2009, $127,000 in 2008 and $36,000 in 2007. Additionally, in 2008 we expended $5.5 million in connection with our acquisition of a patent

application utilized in Zelrix and a worldwide license in the field of migraine to additional intellectual property.

Financing Activities

Cash used in financing activities was $0.3 million for the three months ended March 31, 2010 and $0.2 million for the three months ended March 31, 2009. These amounts reflect scheduled debt repayments.

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Cash provided by financing activities for the year ended December 31, 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.

Cash provided by financing activities for the year ended December 31, 2008 was $22.4 million, reflecting $23.2 million of net proceeds from the sale of Series B preferred stock, partially offset by scheduled debt repayments of $0.9 million.

Cash provided by financing activities for the year ended December 31, 2007 was $7.3 million, reflecting $5.0 million of net proceeds from the sale of Series B preferred stock and $2.4 million, net of issuance costs, from a term loan that we entered into in 2007, partially offset by scheduled debt repayments of $0.1 million.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements, except for operating leases, or relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities.

Contractual Obligations

The following table summarizes our contractual obligations as of December 31, 2009:

	Payments Due by Period				
Contractual Obligations[1]	**Total**	**2010**	**2011 and 2012**	**2013 and 2014**	**2015 and Thereafter**
			(In thousands)		
Debt obligations[2]	$ 818	$ 818			
Interest payments on debt	42	42			
License maintenance fees[3]	330	30	$ 100	$ 100	$ 100
Operating lease obligations	1,143	346	708	89	
Development expenditures[4]	1,750	250	500	500	500
	$ 4,083	$ 1,486	$ 1,308	$ 689	$ 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.

Additionally, this table does not include payments due under an agreement we entered into with LTS as of June 1, 2010, pursuant to which we agreed 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 June 30, 2010, 3.8 million, or approximately $4.7 million based on exchange rates in effect as of June 30, 2010, are to be paid in the remaining monthly installments under this agreement. The terms of this agreement are described in more detail under Business License, Development and Commercial Agreements LTS Lohmann Therapie-Systeme AG.

(2)

This table does not reflect the $10.1 million outstanding principal balance under the April 2010 Convertible Notes and the $5.0 million outstanding principal balance under the May 2010 Loan Facility. Outstanding principal and accrued interest under the April 2010 Convertible Notes automatically convert into shares of common stock upon the closing of this offering. The terms of the repayment of the May 2010 Loan Facility are described in more detail under Liquidity and Capital Resources Debt Facilities.

(3) Under an agreement with 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. In 2010, the annual fee is $30,000. After 2010, the annual fee is $50,000. Because we cannot currently estimate when the first sale of a licensed product will occur, the table reflects payments only through 2016.

(4) Under the agreement with Penn discussed in footnote 3 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 2016.

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 first achievement of specified development, regulatory and sales level milestones related to the first clinical indication approved by a regulatory authority for NP201, our product candidate that is covered by the agreement. 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.

Recent Accounting Pronouncements

We have adopted new accounting guidance on fair value measurements effective January 1, 2008, for financial assets and liabilities. In addition, effective January 1, 2009, we adopted this guidance as it relates to nonfinancial assets and liabilities that are not recognized or disclosed at fair value in the financial statements on at least an annual basis. This guidance defines fair value as the price that would be received to sell an asset or paid to transfer a liability, referred to as the exit price, in an orderly transaction between market participants at the measurement date. The guidance outlines a valuation framework and creates a fair value hierarchy in order to increase the consistency and comparability of fair value measurements and the related disclosures. The adoption of this guidance did not have a material impact on our financial statements.

In June 2008, the Financial Accounting Standards Board, or FASB, issued new guidance related to assessing whether an equity-linked financial instrument (or embedded feature) is indexed to an entity s own stock for the purposes of determining whether such equity-linked financial instrument (or embedded feature) is subject to derivative accounting. We adopted this new guidance effective January 1, 2009. The adoption of this guidance did not have a material impact on our financial statements.

In May 2009, the FASB issued a new standard regarding subsequent events. The standard provides guidance on management s assessment of subsequent events and incorporates this guidance in accounting literature. The guidance is effective prospectively for interim and annual periods ending after June 15, 2009. We adopted this guidance beginning with the interim period ended June 30, 2009. The adoption of this guidance did not have a material impact on our financial statements.

In April 2009, the FASB issued a staff position requiring fair value disclosures in both interim and annual financial statements in order to provide more timely information about the effects of current market conditions on financial instruments. The guidance is effective for interim and annual periods ending after June 15, 2009. We adopted this guidance beginning with the issuance of our September 30, 2009 financial statements. The adoption of this guidance did not have a material impact on our financial statements.

In June 2009, the FASB Accounting Standards Codification, or ASC, was issued, effective for financial statements issued for interim and annual periods ending after September 15, 2009. The ASC supersedes literature of the FASB, Emerging Issues Task Force and other sources. The ASC did not change U.S. generally accepted accounting principles. The adoption of this guidance did not have a material impact on our financial statements.

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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 March 31, 2010, we had cash and cash equivalents of $0.6 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 a manufacturer in Germany. Under one of these agreements, the manufacturer 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 $0.2 million in the three months ended March 31, 2010 to this manufacturer. Under the other agreement, we have agreed to pay the manufacturer an aggregate of 5.4 million in 14 monthly installments that commenced in June 2010, for the purchase of manufacturing equipment for Zelrix, which will be installed in the U.S. As of June 30, 2010, 3.8 million, or approximately $4.7 million based on exchange rates in effect as of June 30, 2010, are to be paid in the remaining monthly installments under this agreement.

Because of these agreements, we are subject to fluctuations in exchange rates. We are currently in the process of transferring our existing manufacturing activities with this manufacturer to the U.S. and anticipate that all of our commercial manufacturing activities will be located in the U.S. following this transfer, thereby substantially eliminating our exposure to fluctuation in the relative values of the U.S. dollar and the Euro.

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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. 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 successfully completed a pivotal Phase III clinical trial for Zelrix in July 2009 and expect to submit a New Drug Application, or NDA, to the United States Food and Drug Administration, or FDA, in the fourth quarter of 2010. Before we submit our NDA, we must complete two ongoing pharmacokinetic trials in healthy subjects and obtain interim data from two ongoing open label Phase III long-term safety trials, or our Phase III safety trials. 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.

Migraine affects approximately 28 million people in the U.S. In 2009, according to IMS Health Inc., or IMS, a leading provider of pharmaceutical industry market data, U.S. sales of prescription products for migraine exceeded $2 billion, over 96% of which were for a class of medication called triptans.

In a majority of their migraines, most migraine patients, or migraineurs, 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 inconsistent efficacy. According to a survey with over 500 respondents conducted by the National Headache Foundation in 2008, 90% of migraineurs have experienced nausea with a migraine and 59% of migraineurs have experienced vomiting with a migraine. In this survey, 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.

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 2009. According to U.S. prescribing information, FDA approved non-oral migraine treatments, limited to nasal spray and injectable formulations, are associated with frequent adverse events. There is no patch approved for the treatment of migraine. We believe that Zelrix will provide an attractive alternative to migraineurs, especially those experiencing nausea and vomiting, inconsistent relief from oral treatments or adverse events associated with triptan use.

In addition to Zelrix, we are developing other product candidates that target opportunities where we believe improved medication delivery can address significant central nervous system medical needs. Based on preclinical testing, we believe that NP201 and NP202, both of which use our long-acting delivery, or LAD, technology, will be able to deliver stable medication levels for multiple months with a single administration.

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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	Expected NDA submission during fourth quarter of 2010. Pivotal Phase III clinical trial completed. Two ongoing Phase III safety trials. Two ongoing pharmacokinetic trials in healthy subjects.
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 28 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 an article, also by Dr. Richard Lipton, published in 2001 in *Headache*, a peer-reviewed medical journal, which we refer to as Lipton, 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.

According to IMS, over 13 million prescriptions for medications indicated for acute migraine were filled in the U.S. in 2009. More than 90% of these prescriptions were for triptans. Triptan sales in the U.S. in 2009 exceeded $2.0 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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Treatment of Acute Migraine

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

Triptans, including a triptan combination;

Ergotamines and 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 widely prescribed triptan, according to IMS.

The following table summarizes U.S. unit and dollar sales information for 2009, 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	2009 Units Sold[1] (% Total)	2009 Sales (% Total)
Triptan	Generic sumatriptan and Imitrex Maxalt (rizatriptan) Zomig (zolmitriptan) Relpax (eletriptan) Treximet (sumatriptan/naproxen)	Tablet, orally disintegrating tablet, nasal spray, injection	122.9 million (69.2%)	$2.1 billion (96.8%)
Analgesic Combination	Epidrin, Midrin, Migrazone and generics (isometheptene mucate, dichloralphenazone, acetaminophen) Prodrin (acetaminophen, caffeine, isometheptene)	Capsule	48.4 million (27.2%)	$15.0 million (0.7%)
Ergotamine	Migranal (dihydroergotamine) DHE-45 and generics (dihydroergotamine) Cafergot and generics (dihydroergotamine, caffeine)	Nasal spray, injection, tablet suppository	6.4 million (3.6%)	$54.4 million (2.5%)

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

As of June 30, 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 2009, 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 consists of a controlled delivery technology that 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. A small light on the patch indicates that the patch is delivering medication. Zelrix actively delivers sumatriptan for four hours. The patient may remove the patch whenever convenient after the dosing period.

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 alternative for migraineurs suffering from nausea or vomiting who might otherwise delay or avoid taking medication.

Increasing consistency of response. Zelrix does not depend on gastrointestinal absorption. As a result, we believe that Zelrix will provide more consistent relief than oral triptans.

Minimizing triptan adverse events. Zelrix tightly controls the delivery of sumatriptan. As a result and based on our clinical trial experience, we believe that Zelrix use will result in a low incidence of triptan adverse events while effectively treating migraine.

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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 expect to submit an NDA for Zelrix to the FDA in the fourth quarter of 2010 under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, or FDCA. In addition to our Zelrix data, under Section 505(b)(2), our NDA submission will rely on existing published data and the FDA s previous finding of the safety and effectiveness of Imitrex. Before submitting our NDA, we are required to complete our two ongoing pharmacokinetic trials in healthy subjects and obtain interim data from our two Phase III safety trials as described below.

Our clinical trial program for Zelrix consists of:

Six completed Phase I clinical trials;

One completed pivotal Phase III clinical trial;

Two ongoing pharmacokinetic trials in healthy subjects; and

Two ongoing Phase III safety trials.

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.

As part of our NDA submission for Zelrix, the FDA indicated that it will require that we provide long-term clinical data for patients treated for six months and patients treated for one year. We plan to conduct an interim analysis of data from patients enrolled in our Phase III safety trials in order to be able to include these required data in our NDA submission.

In addition, because Zelrix will be applied to the skin, the FDA may require that we conduct a skin sensitization study. In July 2010, the FDA notified us that the skin sensitization data being collected during our two Phase III safety trials has the potential to be sufficient, subject to review by the FDA as part of the NDA for Zelrix, without the need to conduct a separate skin sensitization study. Depending on the outcome of the FDA s review, we may be required to conduct the separate skin sensitization study. We believe, however, that the skin sensitization data from our two Phase III safety trials will be sufficient.

The FDA also requested that we provide data in our NDA regarding an *in vitro* analytical testing method for Zelrix to confirm the amount of medication delivered. An *in vitro* analytical test is usually conducted on artificial tissue. To date, we have not successfully developed this test because Zelrix is designed to operate only on living tissue. We are working with the FDA to develop acceptable alternatives.

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.

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

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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 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.

Ongoing Open Label Phase III Long-Term Safety Trials

We are conducting two Phase III safety trials, both of which we initiated in the first quarter of 2009, to 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. These two trials are fully enrolled with a

total of 714 patients at 34 investigative sites in the U.S. As of June 30, 2010, we had treated over 6,250 migraines with Zelrix in these trials.

As part of our NDA submission for Zelrix, the FDA indicated that it will require that we provide long-term clinical data for patients treated for six months and patients treated for one year. We plan to conduct an interim analysis of data from patients enrolled in our Phase III safety trials in order to be able to include these required data in our NDA.

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Phase I Clinical Trials

We have completed six 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

Adverse Event		Number of Subjects Reporting Event (%)							
Categorization	Preferred Term	Injection (23 Subjects)		Oral (23 Subjects)		Nasal Spray (23 Subjects)		Zelrix (17 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.

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Ongoing Pharmacokinetic Trials in Healthy Subjects

We are conducting two additional pharmacokinetic trials in healthy subjects. One is designed to evaluate the pharmacokinetics of Zelrix in the young and elderly; the other is designed to evaluate the bioavailability of Zelrix. Each clinical trial will enroll approximately 60 subjects and must be completed prior to submitting our NDA.

Skin Irritation Study

In July 2010, we initiated a study of Zelrix to evaluate the skin irritation profile of the Zelrix patch. The study is designed to enroll 30 healthy adult subjects at one investigative site in the U.S. and to measure the amount of skin irritation resulting from repeated application of Zelrix. As of July 20, 2010, the study has enrolled ten healthy adult subjects. In July 2010, the FDA notified us that the planned number of subjects and trial design were sufficient to evaluate the irritation potential of Zelrix. We expect to include the skin irritation data as part of our NDA submission for Zelrix.

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, including neurologists, headache specialists and select primary care physicians. 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. According to IMS, 2009 sales of Parkinson s disease therapies in the U.S., European Union and Japan totaled approximately $3.6 billion.

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 of 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.

Only two Parkinson s disease medications currently provide for continuous delivery, and neither is approved in the U.S. Duodopa is a levodopa gel marketed by Solvay S.A. 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 plan to initiate an acute toxicology study for NP201 in the second half of 2010 and 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.

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 own 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.

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, including the incorporation of SmartRelief. We pay fees to LTS for manufacturing development, preparation of manufacturing documentation for our 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 manufacturing equipment for Zelrix. The machinery that LTS will use to produce the commercial supply of Zelrix, if we enter into a commercial manufacturing agreement, will be customized to the particular manufacturing specifications of Zelrix. LTS will design this machinery and assemble it from components manufactured by third party suppliers and paid for by us pursuant to the equipment funding agreement.

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 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.

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 likely would require or encourage use of, and consumers likely would 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.

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 dihydroergotamine, both for acute migraine, and Allergan, Inc. s Botox for chronic migraine. Each of these has either completed or is in Phase III clinical development.

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.

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. In May 2009, Teikoku Pharma USA, Inc. acquired Travanti. Pursuant to the terms of the Travanti agreement, we paid $5.5 million to Travanti 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. 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 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.

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. LTS must use commercially reasonable efforts to provide us with supplies for our clinical trials and also has provided us with supplies for our non-clinical use. We agreed to pay LTS for their services on an hourly basis. As of June 30, 2010, we have incurred fees of $5.3 million under the development and license agreement with LTS, $5.1 million of which have been paid.

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 under the manufacturing agreement between LTS and us. 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.

An invention relating solely to our intellectual property arose in connection with the development and license agreement, and we filed a patent application covering that invention.

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. We have agreed to make installment payments to LTS, in the aggregate amount of 5.4 million in 14 monthly installments that commenced in June 2010, according to an agreed upon payment schedule. As of June 30, 2010, 3.8 million, or approximately $4.7 million based on exchange rates in effect as of June 30, 2010, are to be paid in the remaining monthly installments under this agreement.

Under the agreement, LTS will purchase and install the equipment according to an agreed upon project plan. 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.

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 have paid Penn license initiation, transaction, amendment and maintenance fees totaling $100,000 in the aggregate and must 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.

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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 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.

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 June 30, 2010, we exclusively license one issued U.S. patent and its foreign counterparts, and own six U.S. patent applications, as well as corresponding Patent Cooperation Treaty, or PCT, applications and their foreign counterparts, which relate to Zelrix.

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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 China, Europe and Japan 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 six 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 for an integrated iontophoretic patch, including Zelrix.

Four of the U.S. applications currently have pending international applications. We have corresponding foreign patent applications in Australia, Brazil, Canada, China, Europe, Japan, Mexico, New Zealand, South Africa, Asia, India and Israel for one of these applications. The remaining two U.S. applications are related provisional applications and have yet to be foreign filed. If the four non-provisional U.S. applications and their foreign corresponding applications issue, we generally expect these patents to expire between 2027 and 2029. The two U.S. provisional applications, if pursued in non-provisional and foreign corresponding applications, and if issued, would generally be expected to expire in 2030.

Additionally, as of June 30, 2010, we own or exclusively license one issued U.S. patent and nine 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 seven non-provisional U.S. applications and their corresponding foreign applications, if issued, are generally expected to expire between 2021 and 2027. The remaining two U.S. provisional applications, if pursued in non-provisional and foreign corresponding applications, and if issued, would generally be expected to expire in 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.

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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.

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.

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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.

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. We anticipate that the FDA will grant our product candidates a 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.

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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,