ZOGENIX, INC.
Form 10-K
March 04, 2011
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

Form 10-K

(Mark One)

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

or

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

Commission file number: 001-34962

Zogenix, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**20-5300780**

(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
12671 High Bluff Drive, Suite 200	
San Diego, California (Address of Principal Executive Offices)	**92130** (Zip Code)

858-259-1165

(Registrant s Telephone Number, Including Area Code)

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

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value $0.001 per share	The NASDAQ Global Market

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

None

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

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

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

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

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

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

Large accelerated filer ¨ Accelerated filer ¨ Non-accelerated filer x Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes ¨ No x

As of March 1, 2011, the aggregate market value of the registrant s common stock held by non-affiliates of the registrant was approximately $34,059,988, based on the closing price of the registrant s common stock on the Nasdaq Global Market of $4.24 per share. The registrant has elected to use March 1, 2011 as the calculation date, as on June 30, 2010 (the last business day of the registrant s most recently completed second fiscal quarter) the registrant was a privately-held concern.

The number of outstanding shares of the registrant s common stock, par value $0.001 per share, as of March 1, 2010 was 34,021,483.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant s 2011 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by

reference into Part III of this Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the registrant s fiscal year ended December 31, 2010.

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ZOGENIX, INC.

FORM 10-K ANNUAL REPORT

For the Fiscal Year Ended December 31, 2010

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Sumavel®, DosePro , Intraject® and Zogenix are our trademarks. This Annual Report on Form 10-K also contains trademarks of other companies including Amerge®, Axert®, BOTOX®, Cambia , Frova , Imigran®, Imitrex®, Imitrex STATdose System®, Lortab®, Maxalt®, Relpax®, SODAS®, Treximet , Vicodin®, Voltaren® and Zomig . Unless otherwise specified, all prescription, prescriber and patient data in this Annual Report on Form 10-K is from Wolters Kluwer Pharma Solutions, Source® Pharmaceutical Audit Suite (PHAST), Institutional/Retail, Source® PHAST Retail, Source® Prescriber, Source® LaunchTrac, Source® Dynamic Claims or Source® Lx PTA.

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PART I

Forward-Looking Statements and Market Data

This Annual Report on Form 10-K and the information incorporated herein by reference contain forward-looking statements that involve substantial risks and uncertainties, including statements regarding the future sales potential for Sumavel DosePro, the progress and timing of clinical trials, the safety and efficacy of our product candidates, the goals of our development activities, estimates of the potential markets for our product candidates, estimates of the capacity of manufacturing and other facilities to support our products, projected cash needs and our expected future revenues, operations and expenditures. The forward-looking statements are contained principally in the sections entitled Risk Factors, Management s Discussion and Analysis of Financial Condition and Results of Operations and Business. In some cases, you can identify forward-looking statements by the following words: may, will, could, would, should, expect, intend, plan, anticipate, believe, project, potential, continue, ongoing or the negative of these terms or other comparable terminology, although not all forward-looking statemen contain these words. These statements relate to future events or our future financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. We discuss many of these risks, uncertainties and other factors in this Annual Report on Form 10-K in greater detail under the heading Item 1A Risk Factors.

Given these risks, uncertainties and other factors, we urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. You should read this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. We undertake no obligation to revise or update publicly any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for Sumavel DosePro, ZX002 and other drugs, including data regarding the estimated size of those markets, their projected growth rates, the incidence of certain medical conditions, statements that certain drugs, classes of drugs or dosages are the most widely prescribed in the United States or other markets, the perceptions and preferences of patients and physicians regarding certain therapies and other prescription, prescriber and patient data, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. In particular, unless otherwise specified, all prescription, prescriber and patient data in this Annual Report on Form 10-K is from Wolters Kluwer Pharma Solutions, Source® Pharmaceutical Audit Suite (PHAST) Institution/Retail, Source® PHAST Retail, Source® Prescriber, Source® LaunchTrac, Source® Dynamic Claims or Source® Lx PTA. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

Sumavel®, DosePro , Intraject® and Zogenix are our trademarks. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

Unless the context requires otherwise, references in this Annual Report on Form 10-K to Zogenix, we, us and our refer to Zogenix, Inc., including, as of June 7, 2010, its consolidated subsidiary.

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Item 1. Business

Overview

We are a pharmaceutical company commercializing and developing products for the treatment of central nervous system disorders and pain. Our first commercial product, Sumavel® DosePro (sumatriptan injection) Needle-free Delivery System, was launched in January 2010. Sumavel DosePro offers fast-acting, easy-to-use, needle-free subcutaneous administration of sumatriptan for the acute treatment of migraine and cluster headache in a pre-filled, single-use delivery system. Sumavel DosePro is the first drug product approved by the U.S. Food and Drug Administration, or FDA, that allows for the needle-free, subcutaneous delivery of medication. Sumavel DosePro may serve as a treatment alternative to oral and nasal triptans and may offer simple, convenient administration when compared to traditional, needle-based sumatriptan injection. As a result, we believe that Sumavel DosePro has the potential to be prescribed by a broad physician audience, especially for difficult to treat migraine episodes. Total U.S. gross sales to wholesalers of Sumavel DosePro through December 31, 2010 were $25.3 million. For the same period, we recognized $18.7 million in net product revenue from these sales, represented by more than 35,200 aggregate dispensed prescriptions.

Migraine is a syndrome that affects approximately 30 million people in the United States, according to a 2010 National Headache Foundation, or NHF, press release. Triptans are the class of drugs most often prescribed for treating migraines. In the United States in the 12 months ended December 2010, triptans generated sales of approximately $3.5 billion and sumatriptan, including branded and generic forms, represented the biggest market share of the seven approved triptans, with sales of approximately $2.1 billion, according to Wolters Kluwer Pharma Solutions (Source® PHAST Institution/Retail).

We launched the commercial sale of Sumavel DosePro in the United States in January 2010 with our co-promotion partner, Astellas Pharma US, Inc., or Astellas. Our sales and marketing organization is comprised of approximately 100 professionals. Our field sales force of approximately 80 representatives is promoting Sumavel DosePro primarily to neurologists and other key prescribers of migraine medications, including headache specialists. Our promotional efforts are complemented by our collaboration with Astellas and approximately 400 of its sales representatives, who are promoting Sumavel DosePro primarily to primary care physicians, OB/GYNs, emergency medicine physicians and urologists in the United States. We also have entered into a partnership for Sumavel DosePro with Desitin Arzneimittel GmbH, or Desitin, to accelerate development and regulatory approvals in Europe and further enhance the global commercial potential of Sumavel DosePro.

We are continuing to promote Sumavel DosePro to new and repeat prescribers in both the neurology and primary care settings, and promoting its use to a range of patient segments, including new triptan users, patients being converted to the product from other migraine drugs and patients who have been prescribed Sumavel DosePro and also have other triptan prescriptions. Through our ongoing efforts with the largest commercial health plans, Sumavel DosePro is achieving broad coverage in the United States, with a reimbursement claims approval rate of approximately 80% since launch (Source® Dynamic Claims January 2010 December 2010).

Our lead product candidate, ZX002, is a novel, oral, single-entity controlled-release formulation of *hydrocodone* currently in Phase 3 clinical trials for the treatment of moderate to severe chronic pain in patients requiring around-the-clock opioid therapy. ZX002 utilizes Elan Pharma International Limited s, or Elan s, proprietary Spheroidal Oral Drug Absorption System, or SODAS technology, which provides consistent 12-hour pain relief relative to existing immediate-release combination formulations. Most marketed *hydrocodone* products contain the analgesic combination ingredient *acetaminophen,* which if taken in high quantities over time has the potential to cause liver toxicity. ZX002, if approved, may represent the first available controlled-release version of *hydrocodone* and also the first *hydrocodone* product that is not combined with another analgesic. As a result, we believe ZX002 could generate sales from both patients who are using immediate-release opioid products on a chronic basis and patients already using extended-release opioids. We initiated the Phase 3 clinical development program for ZX002 in March 2010 and, if successful, expect to submit a New Drug Application, or NDA, with the FDA by early 2012. We in-licensed exclusive U.S. rights to ZX002 from Elan in 2007.

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The American Pain Society estimated in 1999 that 9% of the U.S. adult population suffers from moderate to severe non-cancer related chronic pain. Chronic pain can be treated with both immediate-release and extended-release opioids. We define our target market for ZX002 as prescription, non-injectable *codeine*-based and extended-release *morphine*-based pain products. This market generated U.S. sales of approximately $13.5 billion for the year ended December 2010, based on average wholesale price, on approximately 206 million prescriptions. During the same period, existing *hydrocodone* products, the most commonly prescribed pharmaceutical products in the United States, generated $3.2 billion in sales on approximately 128 million prescriptions. (Source® PHAST Retail). We believe ZX002 has the potential to be an important therapeutic alternative to existing *hydrocodone* products, including the branded product Vicodin and its generic equivalents.

Our DosePro technology is a novel, patent-protected, needle-free drug delivery system designed for self-administration of a pre-filled, single dose of liquid drug. We believe the FDA s approval of Sumavel DosePro represents an important validation of the technology. Results from our pre-clinical and clinical studies demonstrate that DosePro can be used successfully with small molecules and biological products, including protein therapeutics and monoclonal antibodies. We are building our internal product pipeline by investigating proven drugs that can be paired with DosePro to enhance their benefits and commercial attractiveness. Specifically, we have initiated pre-clinical development on a proprietary long-acting formulation of an injectable central nervous system, or CNS, drug product and are also evaluating the market potential, formulation requirements and clinical development pathway of an additional CNS compound that could be paired with DosePro to enhance its commercial attractiveness. If these efforts are successful, we may be able to submit an Investigational New Drug Application, or IND, for one or both product candidates in 2011. We are also seeking to capitalize on our DosePro technology by out-licensing it to potential partners enabling them to enhance, differentiate or extend the life cycle of their proprietary injectable products.

Our Strategy

Our core strategy is to commercialize and develop differentiated CNS and pain therapeutics that can address significant unmet medical needs and overcome limitations of existing products. Key elements of our strategy include:

Increasing sales and continuing to drive patient and physician adoption of Sumavel DosePro in the United States. Total U.S. net product revenue from sales of Sumavel DosePro through December 31, 2010 were $18.7 million. We continue to leverage our established commercial infrastructure, our collaboration with Astellas and our investment in sales and marketing programs to help increase awareness and adoption of, and access to, Sumavel DosePro with prescribers, patients, third-party payors, pharmacists and employers.

Developing and commercializing ZX002 for the treatment of moderate to severe chronic pain. Our ongoing Phase 3 clinical program for ZX002 is focused on establishing safety and efficacy of controlled-release single-entity *hydrocodone* to treat moderate to severe chronic pain in patients requiring around-the-clock opioid therapy. If our clinical program is successful and we receive FDA approval, we intend to expand our sales and marketing infrastructure, including expanding our field sales force to 250 or more representatives, to allow us to reach a broad range of opioid prescribers in our target market.

Expanding our product pipeline in CNS disorders and/or pain. We are utilizing our proprietary DosePro technology to add to our internal product pipeline. We have initiated pre-clinical development work on a proprietary long-acting formulation of an injectable CNS drug product and are also evaluating the market potential, formulation requirements and clinical development pathway of an additional CNS compound that could be paired with DosePro to enhance the compound s commercial attractiveness. If these efforts are successful, we may be able to submit an IND for one or both product candidates in 2011.

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Obtaining regulatory approvals for Sumavel DosePro outside of the United States. We have a partnership for Sumavel DosePro with Desitin in order to accelerate development and regulatory approvals in Europe and enhance the global commercial potential of Sumavel DosePro. Desitin received marketing approval from Denmark in November 2010 followed by approvals in Germany, Sweden, Norway and the United Kingdom. We also continue to evaluate potential partnerships to commercialize Sumavel DosePro in additional markets outside of Europe and the United States.

Out-licensing our proprietary DosePro technology. We are evaluating opportunities to out-license the DosePro needle-free drug delivery technology to partners seeking to enhance, differentiate or extend the life-cycle of their injectable products. These opportunities include biologics and small molecules that are both currently marketed products and development stage product candidates.

Securing rights to complementary products and product candidates that address CNS disorders and/or pain. To strategically leverage our commercial resources and generate additional revenue, we are seeking third-party co-promotion opportunities. In the future, we will also consider in-licensing or acquisition opportunities with a focus on product candidates that utilize novel technologies to improve the profile of existing compounds for CNS disorders and/or pain.

Our Product and Product Candidates

Sumavel DosePro for the Acute Treatment of Migraine and Cluster Headache

We launched the commercial sale of Sumavel DosePro in the United States in January 2010 with our co-promotion partner, Astellas. Our Sumavel DosePro (sumatriptan injection) Needle-free Delivery System offers fast-acting, easy-to-use subcutaneous administration of sumatriptan for the acute treatment of migraine and cluster headache. Sumavel DosePro utilizes our proprietary DosePro system which enables patients to self-administer subcutaneous sumatriptan in three easy steps. Sumavel DosePro may serve as a treatment alternative to oral and nasal triptans and may offer simple, convenient administration when compared to traditional, needle-based sumatriptan injection. As a result, we believe that Sumavel DosePro has the potential to be prescribed by a broad physician audience, especially for difficult to treat migraine episodes.

Migraine Market

Migraine is a chronic neurovascular disorder characterized by episodic attacks. According to a 2007 press release from the NHF, approximately 30 million people in the United States suffer from migraines, with women three times more likely to suffer migraines than men. Migraine attacks typically manifest themselves as moderate to severe headache pain, with symptoms that often include nausea and/or vomiting and abnormal sensitivity to light and sound. Migraines can severely limit the normal daily functioning of patients, who may seek dark, quiet surroundings until the episode has passed. According to the International Headache Society, the duration of untreated or unsuccessfully treated migraine episodes ranges from four to 72 hours. According to data published in the March 2002 issue of Neurology, 63% of patients suffer one or more attacks per month, 25% of patients have one or more attacks per week and the median duration of an untreated migraine is approximately 24 hours. Overall, the cost burden of migraine in the United States was estimated by Thomson Medstat in June 2006 to approach $25 billion annually, including $12.7 billion in direct medical costs and $12 billion in indirect costs related to employee absenteeism, short-term disability and workers compensation costs to employers.

Cluster headaches are characterized by groups or clusters of debilitating headaches lasting weeks or months, then disappearing for months or years. This type of headache affects an estimated one million sufferers in the United States, and approximately 90% of these sufferers are male, according to the NHF website. Due to the severe nature of cluster headache, patients are commonly treated with prescription medication.

Acute therapies dominate the prescription migraine and cluster headache market and are used during intermittent attacks. The goals of acute therapy are to stop the attack quickly and consistently, minimize the use of backup and rescue medications, enhance self-care and restore the patient s ability to function, use the least amount of medication and limit adverse side effects.

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A major advancement in the acute treatment of migraine began in 1993 with the launch of the first triptan, sumatriptan injection (Imitrex), in the United States. All triptans are selective agonists for the 5-HT_{1B} and 5-HT_{1D} receptors. Triptans presumably exert their antimigrainous effect through binding to vascular 5-HT_1 receptors, which have been shown to be present on both the human basilar artery, one of the major arteries that supplies blood to the brain, and the outer most membrane covering the brain. Triptans activate these receptors to cause vasoconstriction, an action in humans correlated with the relief of migraine and cluster headache. Sumatriptan was subsequently joined by other drugs in the triptan class. By the year 2003, there were seven approved triptans in the United States with a focus on oral delivery forms to offer convenience of dosing for migraine patients. Sumatriptan is the only triptan available in oral, nasal and subcutaneous forms, each of which has different pharmacokinetic properties.

Triptans remain the drugs of choice and the most often prescribed therapy for the acute treatment of migraine and cluster headache. The following table provides a breakdown of the U.S. triptan market, including sales and doses prescribed for oral (tablets and melts), nasal and injectable forms of triptan for the 12 months ended December 2010.

U.S. Triptan Market

(12 months ended December 2010)

Triptan Form	Sales (millions)	$ Share	Doses (millions)	Dose Share
Oral Tablet	$ 2,734	77.7%	112.6	85.0%
Oral Melt	354	10.0	13.4	10.2
Nasal	113	3.2	3.0	2.2
Injectable	318	9.1	3.5	2.6
Total	$ 3,519	100%	132.5	100%

Source® PHAST Institution/Retail.

As indicated in the prior table, the triptan market is dominated by oral dosage forms (tablets and melts), with approximately 95% of U.S. triptan doses taken as oral formulations and the remaining 5% split between injectable and nasal formulations. Branded and generic *sumatriptan*, in all dosage forms, remains the most prescribed triptan molecule with sales of approximately $2.08 billion (59% dollar share of the triptan market). Of that amount, the injectable forms of sumatriptan accounted for $319 million. By comparison, ergotamine agents, another class of drugs used for the acute treatment of migraine, including injectable DHE and Migranal, accounted for $55.3 million in sales in the United States during the same 12-month period. (Source® PHAST Institution/Retail). Sumatriptan is the only triptan available to patients in the injectable form and, with the exception of Sumavel DosePro, all other forms of injectable sumatriptan make use of needle-based injections for their administration.

In five major European countries (France, Germany, Italy, Spain and the United Kingdom), triptans generated total sales of approximately $550 million for the 12 months ended June 2007, according to average wholesale price data published by IMS Health MIDAS. Of that $550 million, the European equivalent of Imitrex, Imigran, represented sales of approximately $148 million, of which the injectable form accounted for approximately $35 million.

Migraine Market Dynamics

The type of migraine treatment utilized by patients often depends on the frequency and severity of the headache, its speed of onset and previous response to medication. In published studies, migraine sufferers most often cite faster onset of pain relief as a key therapeutic attribute they would like from their migraine medication.

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Patients with more frequent or severe migraines or those who do not respond to simple analgesics may seek medical attention with a primary care physician initially and then with a headache clinic or neurology specialist if needed. Once a physician makes a diagnosis of migraine, oral triptans are generally prescribed as first-line therapy.

If a patient does not respond to one triptan product, the physician may switch to another triptan or dosage form or add another triptan or dosage form to a patient s treatment armamentarium. Market research conducted on our behalf by Boston Healthcare Associates, Inc. indicates that it is common for a migraine patient to be offered several different oral triptan options before being offered a nasal or injectable product. In addition, the same market research indicates that approximately 25% of migraine patients had two or more active prescriptions for different brands and/or forms of triptan therapy. We believe these patients maintain multiple prescriptions because they have found that certain medications or dosage forms work better for certain types of migraines and choose which medication to use based on the type of migraine episode they are experiencing.

Clinical research has substantiated that the nature of migraine episodes varies widely. In some episodes, patients can sense a migraine coming and take their medication accordingly. In other episodes, patients may wake up with a migraine already in progress or the migraine may come on suddenly. An estimated 48% of migraines occur between the hours of 4:00 a.m. and 9:00 a.m., according to an article published in the June 1998 issue of Headache. Migraines may also be associated with nausea and/or vomiting. Twenty-nine percent of patients reported vomiting as a symptom of migraine attacks, according to the American Migraine Study II, and epidemiological studies in migraine reveal that over 90% of patients have experienced nausea during a migraine attack and more than 50% have nausea with the majority of attacks, according to an article published in Drugs in 2003 (Volume 63, Issue 21). Depending on the type of migraine episode, a treatment may be more or less effective. For example, oral treatments may be of little value in a patient who is vomiting or who is experiencing migraine-associated gastric stasis. There is also clinical evidence that oral agents may be less effective when taken at a later stage of a migraine attack, rather than at an earlier stage. Consequently, rapid onset migraine and waking with a migraine attack may reduce the benefits to patients of oral triptans, because both represent fully-developed attacks.

The following table compares the time to maximum drug concentration in blood, or Tmax, and pain relief of oral forms, including melts and tablets, and nasal forms of marketed triptans to sumatriptan injection. The data are derived from Prescribing Information for the different formulations of these marketed triptans:

Triptan Prescribing Information Data

Form/Product (API)	Tmax	Relief at 1 hour(1)(2)	Relief at 2 hours(2)
Subcutaneous			
Sumavel DosePro (sumatriptan injection)	12 minutes	70%	81-82%
Nasal			
Imitrex (*sumatriptan*)	Not provided	38-46%	43-64%
Zomig (*zolmitriptan*)	3.0 hrs	60%	69-70%
Oral Melt			
Zomig-ZMT (*zolmitriptan*)	3.0 hrs	33-43%	63%
Maxalt-MLT (*rizatriptan*)	1.6-2.5 hrs	38-43%	59-74%
Oral Tablets			
Imitrex (*sumatriptan*)	2.0-2.5 hrs	28-36%	50-62%
Treximet (*sumatriptan/naproxen sodium*)	1.0 hrs	28%	57-65%
Zomig (*zolmitriptan*)	1.5 hrs	35-45%	59-67%
Maxalt (*rizatriptan*)	1.0-1.5 hrs	38-43%	60-77%
Amerge (*naratriptan*)	2.0-3.0 hrs	19-21%	50-66%(3)
Axert (*almotriptan*)	1.0-3.0 hrs	32-36%	55-65%
Frova (*frovatriptan*)	2.0-4.0 hrs	12%	37-46%
Relpax (*eletriptan*)	1.5 hrs	20-30%	47-77%

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(1) Other than Sumavel DosePro (sumatriptan injection), we have estimated one-hour pain relief data for all forms/products based on Kaplan-Meier plots included in each product s Prescribing Information of the probability over time of obtaining headache response following treatment.
(2) Range reflects headache relief data obtained in placebo controlled clinical studies, which include different doses of the same triptan.
(3) Represents pain relief at four hours.

Tmax closely correlates to speed of onset of pain relief, and has also been shown to be correlated with completeness of pain relief and pain freedom over time. Relief at two hours is the standard endpoint used in migraine studies and represents the percentage of patients reporting a reduction of migraine symptoms from a classification of severe or moderate to mild or none within two hours after taking the medication. As indicated in the prior table, sumatriptan injection has the earliest Tmax, reaching maximum blood concentration in 12 minutes, as compared with one or more hours for the other marketed triptan products, and exhibits the highest percentage of patients reporting pain relief at two hours (81%-82%) as compared to all other marketed oral and nasal triptan products (37-77%). Sumatriptan injection is the only migraine product that explicitly reports pain relief at one hour in its Prescribing Information. The efficacy profile of sumatriptan injection has been suggested to be related to its faster rate (not extent) of drug absorption compared to oral and nasal forms of triptans. Nasal forms, while claimed by some to be fast-acting, have drug absorption profiles similar to oral forms because a large portion of the administered dose is usually swallowed prior to absorption.

Unmet Needs in Acute Migraine Therapy

Triptans have been widely used in clinical practice for more than 15 years and are generally considered to be safe and effective for many patients during their migraine episodes. However, more than half of all patients are unsatisfied with their current migraine therapy, as reported from a national survey of 500 migraine sufferers published by the NHF in June 2010 and supported by a grant from us and Astellas. Specifically, the NHF survey results indicate that three in four migraine sufferers said that their current medication did not work fast enough to get them back to their life when a migraine strikes suddenly or upon waking, and a majority of migraine sufferers said their prescription oral migraine medication was not useful for every migraine attack. Limitations of oral and nasal triptan formulations include:

Slower onset of pain relief. As shown in the prior table, compared to Sumavel DosePro, each oral and nasal triptan has a longer Tmax, which is correlated with a slower onset of pain relief.

Lower degree of pain relief. As shown in the prior table, oral and nasal triptans may have a lower percentage of patients reporting pain relief at one and two hours following treatment as compared to Sumavel DosePro.

Significant numbers of non-responders. According to our market research with physicians and patients, approximately 30% of migraine patients fail to respond to an oral or nasal triptan.

Nasal route unpleasant. The nasal route is an alternative to oral delivery; however, nasal spray can be unpleasant in taste.

Some of these limitations are more pronounced depending on the type of migraine episode the patient is suffering. For example, when waking with a migraine already in progress, speed to onset of pain relief is important. In migraines with nausea and/or vomiting, a patient may not be able to ingest an oral treatment.

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Despite its speed of onset and completeness of pain relief advantages over oral and nasal triptans, needle-based sumatriptan injection has been limited to less than 10% of the U.S. triptan market on a dollar basis and less than 3% on a total dose basis (Source® PHAST Institution/Retail) January 2010 December 2010**).** We believe this is largely due to limitations related to its delivery system which include:

Needle-based. Approximately 50% of patients refuse to use a needle-based injectable product for migraine because of needle anxiety or fear, or a lack of confidence in their ability to administer an injection correctly, according to physician market research conducted in 2006 by Palace Healthcare Group, Inc. on our behalf.

Cumbersome to use. The Imitrex STATdose System, or Imitrex STATdose, GSK s autoinjector for delivering sumatriptan with a needle, and its generic equivalents require more than 15 steps per their published instructions to prepare, administer and reload for its next use. This multi-step process, which patients have to complete during a migraine episode, is prone to error. Further, market research conducted by Palace Healthcare Group on our behalf finds that physicians report that the training required for Imitrex STATdose is a barrier to prescribing.

Needlestick risk. Needle-based systems may require special handling and needle disposal, or sharps, containers to avoid needlestick injuries.

Due to these limitations, there has historically been a limited prescriber base for injectable delivery forms of sumatriptan. Of an aggregate of over 350,000 prescribers of triptans in the United States, only an approximate 67,000 had written a prescription for sumatriptan injection (including Sumavel DosePro) in the 12 months ended December 2010 (Source® Prescriber January 2010 December 2010. As a result, a limited number of patients are offered injectable delivery forms. Only 54% of migraine patients had ever been offered sumatriptan injection according to patient market research conducted by Boston Healthcare Associates, Inc. on our behalf.

Our Solution: Sumavel DosePro

Sumavel DosePro is a pre-filled, single-use disposable, needle-free drug delivery system that subcutaneously delivers 6 mg of *sumatriptan* in 0.5 mL of sterile liquid. Sumavel DosePro was designed to be portable, intuitive and easy-to-use. To use, the patient simply snaps off a plastic tip, flips back a lever and presses the end of the delivery system to the skin of the abdomen or thigh. Under the force of a small amount of compressed nitrogen gas, the liquid form of sumatripta*n* is expelled out of the device as a thin jet of medication, which pierces the skin and selectively deposits into the subcutaneous tissue. This process occurs in less than 1/10th of a second.

Due to its unique attributes, Sumavel DosePro has the potential to expand the dosage share for injectable sumatriptan beyond the traditional needle-based forms because it reduces the barriers inherent in needle-based delivery systems to being prescribed by physicians and accepted by patients. Sumavel DosePro may provide patients with the following benefits when compared to alternative triptan formulations:

Rapid, more complete, migraine pain relief. Sumavel DosePro can provide onset of migraine pain relief in as little as ten minutes for some patients, according to its Prescribing Information. The Prescribing Information for the product indicates that an average of 81% (vs. an average of 34% for placebo) of patients show pain relief at two hours following administration of Sumavel DosePro and that 49% of patients were pain free within 1 hour (vs. 9% for placebo) and 64% were pain free within two hours (vs. 15% for placebo) following administration.

Help for sufferers of morning migraines, fast onset migraine and migraines with vomiting. According to two studies published in the October 2006 issue of Clinical Therapeutics, 48% and 57% of patients with waking migraines were pain free at two hours (vs. 18% and 19% for placebo) following administration of sumatriptan injection. Subcutaneous sumatriptan is also as efficacious when administered early during a migraine attack as when the attack is full-blown. In addition, the pharmacokinetics of subcutaneously delivered sumatriptan is not affected by gastric stasis, nausea and/or vomiting.

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Help for triptan tablet non-responders. Clinical research published in the January 2007 issue of Journal of Headache and Pain suggests injectable sumatriptan provides relief in up to 90% of migraine patients who have not responded to oral tablet triptans in at least two of their last three migraines. In this study, 43 patients who had failed to respond to oral triptans in at least two of their last three migraines were given sumatriptan injection for their next migraine. Of these patients, 91% reported pain relief at two hours, 56% reported being pain free at two hours and 32% reported sustained pain freedom through 24 hours following treatment of their first headache.

Simplicity, through a new, convenient and easy-to-use option. Sumavel DosePro is based on our unique delivery system which was designed to be portable, intuitive and easy-to-use, and can be disposed following use without the need of a sharps container. We believe healthcare providers appreciate the simplicity of DosePro because it is easy to train patients to use properly. Our usability study of Sumavel DosePro showed 98% of patients were able to self-administer Sumavel DosePro in the home during an acute migraine attack, without clinical supervision and with minimal prior training.

Needle-free, eliminating needle-based issues. Because it is needle-free, we believe Sumavel DosePro may eliminate the basis for patient needle phobia and fear. Additionally, it removes the risks of needlestick injury, the cost and inconvenience of needle disposal, issues resulting from poor injection technique and costs associated with professionally administered needle-based injections. Studies show when a choice between needle-based and needle-free injection is available, the majority of patients prefer needle-free injection. More specifically, in a head-to-head study conducted by GSK of Sumavel DosePro versus the European branded version of Imitrex STATdose, a needle-based delivery system, 61% of migraine patients preferred using Sumavel DosePro while only 18% preferred using the European branded version of Imitrex STATdose, with the remaining patients expressing no preference.

In addition, we believe that the unique attributes of Sumavel DosePro have the potential to reduce productivity loss in the workplace for patients suffering from migraine. According to a study published in the May 1998 issue of Archives of Internal Medicine, results from a placebo-controlled clinical study of 135 patients having migraine indicated that use of sumatriptan injection may reduce migraine-associated productivity loss. This decrease is a function of both a reduction in time lost due to reduced effectiveness while working and a reduction in time lost due to missing work altogether. Moreover, 52% of patients using sumatriptan injection (vs. 9% for placebo) returned to normal work performance within two hours after dosing.

Sumavel DosePro Commercialization Strategy

Working in collaboration with our co-promotion partner, Astellas, as well as third-party advertising and market research organizations, we developed and are executing a sophisticated and comprehensive commercialization strategy for Sumavel DosePro supported by a range of marketing programs. This strategy and tactical plan was built taking into consideration the unmet needs in the migraine market in conjunction with the unique product attributes of Sumavel DosePro. Key objectives of our commercialization strategy are to:

validate the unmet needs of patients during challenging migraine episodes and position Sumavel DosePro as an effective treatment solution with key prescribers;