Zosano Pharma Corp
Form 10-K
March 29, 2016
Table of Contents

Index to Financial Statements

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2015

or

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

Commission File Number 001-36570

ZOSANO PHARMA CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**45-4488360**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

34790 Ardentech Court

Fremont, CA 94555

(Address of principal executive offices) (Zip Code)

(510) 745-1200

(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 $0.0001 per share	The NASDAQ Capital Market

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

None

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or 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 ¨	Accelerated filer ¨
Non-accelerated filer ¨ (do not check if a smaller reporting company)	Smaller reporting company x

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

The aggregate market value of voting stock held by non-affiliates of the registrant on June 30, 2015 (the last business day of the registrant s most recently completed second quarter) was approximately $36,760,000.

As of March 10, 2016, the registrant had a total of 11,967,895 shares of its common stock, $0.0001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

No documents are incorporated by reference into this Annual Report on Form 10-K.

Table of Contents

Index to Financial Statements

Zosano Pharma Corporation

Annual Report on Form 10-K

For the Fiscal Year ended December 31, 2015

TABLE OF CONTENTS

Table of Contents

Index to Financial Statements

Cautionary Note Regarding Forward-Looking Statements

This report includes forward-looking statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends affecting the financial condition of our business. Forward-looking statements should not be read as a guarantee of future performance or results, and will not necessarily be accurate indications of the times at, or by, which such performance or results will be achieved. Forward-looking statements are based on information available at the time those statements are made and/or management s good faith belief as of that time with respect to future events, and are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in or suggested by the forward-looking statements.

Forward-looking statements include all statements that are not historical facts. In some cases, you can identify forward-looking statements by terms such as may, will, should, could, would, expect, intend, seek, believe, estimate, project, predict, potential, or the negative of those terms, and similar expressions and comp terminology intended to reference future periods. Forward-looking statements include, but are not limited to, statements about:

- the anticipated timing, costs and conduct of our planned clinical trials and preclinical studies, as applicable, for our ZP-PTH, ZP-Glucagon and ZP-Triptan product candidates;
- our expectations regarding the clinical effectiveness of our product candidates;
- the ability to obtain and maintain regulatory approval of our product candidates, and the labeling for any approved products;
- our manufacturing capabilities and strategy;
- our expectations regarding our expenses and revenue, the sufficiency of our cash resources and needs for additional financing;
- our intellectual property position and our ability to obtain and maintain intellectual property protection for our product candidates;
- our expectations regarding competition;
- the anticipated trends and challenges in our business and the markets in which we operate;

the scope, progress, expansion, and costs of developing and commercializing our product candidates;

the size and growth of the potential markets for our product candidates and the ability to serve those markets;

the rate and degree of market acceptance of any of our product candidates;

our ability to establish and maintain development partnerships;

our ability to attract or retain key personnel;

our expectations regarding federal, state and foreign regulatory requirements; and

regulatory developments in the United States and foreign countries.

These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties, including those set forth below in Item 1A, Risk Factors, and in our other reports filed with the U.S. Securities Exchange Commission. Given these uncertainties, you should not place undue reliance on these forward-looking statements. These forward-looking statements represent our estimates and assumptions only as of the date of this Annual Report on Form 10-K and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this Annual Report on Form 10-K.

Table of Contents

Index to Financial Statements

PART I

Item 1. BUSINESS.

Overview

We are a clinical stage specialty pharmaceutical company that has developed a proprietary transdermal microneedle patch system to deliver our proprietary formulations of existing drugs through the skin for the treatment of a variety of indications. Our microneedle patch system offers rapid onset, consistent drug delivery, improved ease of use and room-temperature stability, benefits that we believe often are unavailable using oral formulations or injections. Our microneedle patch system has the potential to deliver numerous medications for a wide variety of indications in commercially attractive markets. By focusing our development efforts on the delivery of established molecules with known safety and efficacy and premium pricing, we plan to reduce our clinical and regulatory risk and development costs and accelerate our time to commercialization.

Our short-wear-time transdermal patch consists of an array of titanium microneedles that is coated with our proprietary formulation of a previously approved drug and attached to an adhesive patch. When the patch is applied with our hand-held applicator, the microneedles penetrate the skin, resulting in rapid dissolution and absorption of the drug through the capillary bed. We believe our system enables rapid and consistent delivery of the drug, with therapeutic effect typically occurring within 30 minutes or less, and easy and convenient administration. We focus on developing specific formulations of approved drugs to be administered by our microneedle patch system, for indications in which rapid onset, ease of use and stability offer significant therapeutic and practical advantages. We target indications with patient populations that we believe will provide us with an attractive commercial opportunity. Our product candidate is ZP-Triptan, our proprietary formulation of zolmitriptan, one of a class of serotonin receptor agonists known as triptans used for the treatment of migraine. In November 2015, we announced positive results from our Phase 1 clinical trial of our ZP-Triptan patch, which was conducted in healthy human subjects in Australia. The Phase 1 results demonstrated the fast absorption of ZP-Triptan that is a characteristic of our microneedle patch and applicator system, which we believe can potentially translate to fast pain relief. Recent feedback from the United States Food and Drug Administration, or FDA, on ZP-Triptan s regulatory path has also been encouraging. The agency has indicated that one positive pivotal efficacy study, in addition to the required safety study, would be sufficient for approval of ZP-Triptan for the treatment of migraine.

In light of these encouraging clinical data and the potential to get to an NDA submission in a relatively short timeframe, we recently made the decision to prioritize our clinical development effort on ZP-Triptan and to suspend further development related to our other product candidates, ZP-PTH and ZP-Glucagon, until such time that we can appropriately fund such development through strategic partnerships or additional financing. While we are considering pursuing clinical development of our ZP-Triptan product candidate to a meaningful milestone, we remain open to opportunities with potential strategic partners to ensure our product candidate will receive the best chance of commercial success.

In connection with our decision to concentrate the clinical development of ZP-Triptan, we recently announced that we would streamline our organization to ensure that we effectively use our funds for this purpose. We implemented a workforce reduction of 24 employees, representing approximately 38% of our total workforce, which we expect to reduce our expenses by approximately $2.0 million, net of severance costs, for fiscal year 2016. We expect to reinvest the savings from the workforce reduction in our ZP-Triptan clinical development program.

Our Strategy

Our goal is to make transdermal drug delivery a standard of care for delivering drugs requiring fast onset. The key elements of our strategy are to:

Pursue indications with high unmet medical need and greater probability of clinical, regulatory and commercial success. We focus on indications in which rapid onset, ease of use and stability offer

Table of Contents

Index to Financial Statements

particularly important therapeutic and practical advantages that address unmet needs, that have patient populations large enough to provide us with an attractive commercial opportunity, and where there is currently potential premium pricing.

Maintain focus on effective execution of clinical trials. We believe that timely and efficient execution of our clinical development plans has been critical to our success to date. We intend to continue to maintain, as a primary focus of our efforts, excellence in execution of our clinical development plan for ZP-Triptan while effectively managing our available cash resources.

Build a balanced portfolio of proprietary and partnered programs. We have retained world-wide commercial rights to all of our product candidates. For product candidates that are outside of our immediate and core area of interest, or where a partner can contribute specific expertise, we intend to evaluate collaborations with strategic partners to further the clinical and commercial development of such product candidates. We are continuing our internally funded development efforts with respect to ZP-Triptan, while simultaneously pursuing partnering opportunities for it, as well as our ZP-PTH and ZP-Glucagon programs. We also intend to selectively collaborate with third parties with respect to the delivery of their proprietary drugs using our microneedle patch system.

Continue to refine our next generation drug delivery platform. We believe that each of the currently available methods of drug administration has significant disadvantages. Oral and nasal products are typically characterized by relatively slow onset of action, and the use of injectables can cause discomfort. We intend to continue to refine our next generation microneedle patch system through enhanced portability and improved ease of use.

Our Development Pipeline

We have tested our microneedle patch system in preclinical and clinical proof of concept studies that demonstrated its technical feasibility with approximately thirty compounds, ranging from small molecules to proteins. Based on our research, we believe that our microneedle patch system can be used to deliver treatments for a wide variety of indications beyond those on which we are currently focused, in which our fast onset, room-temperature stability, and ease of use will fill what we believe is a significant unmet need.

The following table summarizes the status of our development programs that we are currently seeking to partner:

Table of Contents

Index to Financial Statements

Our Product Candidate Actively in Development

ZP-Triptan for Migraine

The focus of our development efforts is on our product candidate ZP-Triptan, our proprietary formulation of zolmitriptan, one of a class of serotonin receptor agonists known as triptans, used for the treatment of migraine. Migraine is a debilitating neurological disease, symptoms of which include moderate to severe headache pain, nausea and vomiting, and abnormal sensitivity to light and sound. Our ZP-Triptan microneedle patch is applied to an individual s upper arm to deliver zolmitriptan to the body, with the objective of providing rapid onset relief from headache symptoms.

Large Market and Attractive Treatment Alternative

According to the Migraine Research Foundation, migraine affects 30 million men, women and children in the United States. Most migraines last between four and 24 hours, but some last as long as three days. According to published studies, 63% of migraine patients experience between one and four migraines per month. According to a 2014 study by Global Data Pharma Point, sales of prescriptions for medications indicated for migraine in the United States were approximately $1.9 billion in 2012. Of this amount, $1.1 billion was for triptans.

We believe that each of the currently available methods of administering triptans, including oral, nasal spray, subcutaneous injection and iontophorectic transdermal patch (which is a device that delivers medicine through the skin by a low electrical current), has significant disadvantages. Some migraine patients fail to respond consistently to oral triptans, and oral treatments may be ineffectual for patients who are suffering from the nausea or gastric stasis that can be associated with migraine. Oral, nasal and iontophoretic patch triptan products are also characterized by relatively slow onset of action. Nasal sprays may be unpleasant in taste, and use of injectables can cause discomfort. Because ZP-Triptan has demonstrated fast onset in preclinical studies, does not depend on gastrointestinal absorption, and provides easy, administration, we believe it could provide an attractive alternative to currently marketed triptan products for the treatment of migraine.

Fast Onset Demonstrated

In migraine, time to maximum drug concentration in blood, or T_{max}, 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.

Table of Contents

Index to Financial Statements

The following table compares T_{max} 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:

Products Included:

(1) Nasal: Imitrex (sumatriptan), Zomig (zolmitriptan) Oral Melt: Zomig-ZMT (zolmitriptan) Maxalt-MLT (rizatriptan)
(2) Oral Tablets: Imitrex (sumatriptan), Treximet (sumatriptan/naproxen sodium), Zomig (zolmitriptan) Maxalt (rizatriptan), Amerge (naratriptan), Axert (almotriptan), Frova (frovatriptan), Relpax (eletriptan)
(3) Subcutaneous: Sumavel DosePro (sumatriptan injection), Imitrex (sumatriptan injection)
(4) Tmax achieved in Phase 1 clinical trial for ZP-Triptan 3.8 mg
(5) Average Tmax represents overall average of the midpoint of the range for all products.
(6) Average relief at 2 hours represents overall average of the midpoint of the range for all products. Range reflects headache relief data obtained in placebo controlled clinical studies, which include different doses of the same triptan.
(7) In USD millions / Source: IMS Integrated NPA data, Jan Dec 2012.

Phase 1 Clinical Trial Results

In November 2015, we announced positive results from the Phase 1 clinical trial of our ZP-Triptan patch. This Phase 1 clinical trial of ZP-Triptan was conducted in Australia. The objectives of the Phase 1 clinical study were to evaluate the tolerability and pharmacokinetics of the ZP-Triptan patch in healthy volunteers. The crossover study among 20 healthy volunteers tested five doses of ZP-Triptan compared to an oral administration of zolmitriptan and additionally a subcutaneous injection of sumatriptan. ZP-Triptan demonstrated rapid absorption compared to the zolmitriptan tablet. During the first part of the clinical study, the 20 participants were randomized and received the following treatments: a 0.48 mg ZP-Triptan patch, two 0.48 mg ZP-Triptan patches, a 1.9 mg ZP-Triptan patch, a 2.5 mg oral zolmitriptan tablet, and a subcutaneous injection of 6mg of sumatriptan, a common treatment for migraine headaches. During the second and third parts of the study, subjects received higher doses, consisting of two 1.9 mg ZP-Triptan patches and one 3.8 mg ZP-Triptan patch, respectively, for assessment of tolerability and pharmacokinetics.

Table of Contents

Index to Financial Statements

ZP-Triptan patch was well-tolerated and rapid absorption was observed which we believe may translate to fast pain relief for migraine patients. The Phase 1 results demonstrating the fast absorption of ZP-Triptan that is characteristic of Zosano s microneedle patch and applicator system are illustrated below:

		C_{max} (SD) ng/ml	T_{max} (range) min	AUC_{0-2hr} (SD) ng/ml hour	AUC_{0-last} (SD) ng/ml hour
A	ZP-Triptan 0.48 mg	1.8 (0.53)	20 (2-30)	2.1 (0.73)	2.8 (1.36)
B	ZP-Triptan 2 x 0.48 mg	3.7 (1.05)	20 (2-30)	4.2 (0.95)	6.5 (1.97)
C	ZP-Triptan 1.9 mg	6.8 (2.75)	20 (2-30)	7.4 (2.53)	12.3 (4.31)
F	ZP-Triptan 2 x 1.9 mg	14.6 (4.46)	17.5 (2-30)	16.4 (5.34)	27.8 (9.93)
G	ZP-Triptan 3.8 mg	22.6 (14.00)	15 (2-30)	19.3 (5.37)	31.7 (8.35)
D	Zolmitriptan 2.5 mg Oral Tablet	3.8 (1.51)	60 (30-240)	4.7 (2.24)	22.2 (10.79)

The concentration-time curve during 0-2 hours for all treatments is displayed in the following table:

All treatments were well tolerated and no significant safety issues were identified. The results for the sumatriptan injection were similar to those reported in previous studies.

We believe that the pharmacokinetic and tolerability results in healthy volunteers show that our ZP-Triptan microneedle patch system could provide considerable clinical advantages over zolmitriptan tablets in the treatment of acute migraine. In this Phase 1 pharmacokinetic study, ZP-Triptan demonstrated rapid absorption and reduced metabolism to the active metabolite with the lowered potential for drug-drug interactions and adverse events via a method that does not depend on gastrointestinal absorption or the discomfort of an injection.

Planned Pivotal Efficacy and Safety Trials

We plan to submit an Investigational New Drug (IND) application for ZP-Triptan to the FDA in the second quarter of 2016. Thereafter, we plan to sponsor a U.S. study to evaluate the effectiveness and safety of ZP-Triptan, when used for the acute treatment of migraine.

The first planned study is a multicenter, randomized, placebo-controlled comparison of three doses of ZP-Triptan (1.0 mg, 1.9 mg, and 3.8 mg) and placebo for the treatment of a single migraine attack. The co-primary endpoints for the study are those defined in the October 2014 FDA Draft Guidance Migraine: *Developing Drugs for Acute Treatment* , on pain and most bothersome symptom freedom. Subjects will record their

Table of Contents

Index to Financial Statements

migraine symptoms in a patient diary, prior to treatment, and at varying intervals following treatment, out to 48 hours. Safety will be assessed by adverse events reported and other standard safety measures.

While we are considering pursuing clinical development of our ZP-Triptan product candidate to a meaningful milestone, we remain open to opportunities with potential strategic partners to ensure our product candidate will receive the best chance of commercial success.

Our Partnering Product Candidates

Our clinical trials of product candidates ZP-PTH for the treatment of severe osteoporosis and ZP-Glucagon for the treatment of severe hypoglycemia have also yielded promising clinical data. In light of our decision to prioritize ZP-Triptan, we currently are not devoting substantial resources to further clinical development of ZP-PTH and ZP-Glucagon, and are actively seeking partnering opportunities with them. These product candidates and their clinical progress are described below.

ZP-PTH for Osteoporosis

Our product candidate ZP-PTH is our proprietary formulation of teriparatide, a synthetic form of parathyroid hormone, which we refer to as PTH 1-34, or PTH, which regulates serum calcium, to be administered for the treatment of severe osteoporosis. Osteoporosis is a disease primarily affecting post- menopausal women that is characterized by low bone mineral and structural deterioration of bone tissue, which can lead to an increase in bone fractures. According to the World Health Organization and the International Osteoporosis Foundation, a patient has severe osteoporosis when he or she has a T-score $\leq$-2.5 (meaning that the patient has a bone mineral density, or BMD, that is two and a one-half standard deviations below the mean BMD of an ethnically matched thirty-year old man or woman, as applicable), plus one or more fragility fractures.

We believe that the two main types of osteoporosis drugs currently available in the United States, anti- resorptive agents and an anabolic agent, either have shortcomings in efficacy and safety or often times provide patients with a less than optimal treatment administration experience. Our ZP-PTH product candidate is intended to provide a convenient, easy-to-use, room-temperature-stable alternative for osteoporosis patients. We have developed a daily and a weekly dose regimen of ZP-PTH and have successfully completed a Phase 2 clinical trial on Daily ZP-PTH and a Phase 1 clinical trial on Weekly ZP-PTH.

We completed a Phase 2 clinical trial of Daily ZP-PTH in the United States (in connection with which we submitted an investigational new drug application, or IND, to the United States Food and Drug Administration, or FDA), Mexico and Argentina in 2008, and we held End-of-Phase 2 meetings with the FDA and similar meetings with European regulatory authorities in 2009.

In 2013, we completed a Phase 1 clinical trial of our Weekly ZP-PTH in Australia and the study demonstrated pulsatile performance with all six patch doses, which is a significant factor for anabolic efficacy. We had a pre-IND meeting with the FDA in July 2014 and discussed the clinical study design for a planned Phase 2 study.

We believe that we have made significant progress in the clinical development of our ZP-PTH product candidate. We have retained world-wide commercial rights to both Daily ZP-PTH and Weekly ZP-PTH. We intend to evaluate collaboration with strategic partners to further the clinical and commercial development of Daily ZP-PTH and Weekly ZP-PTH.

Large Osteoporosis Market with Significant Unmet Needs

Osteoporosis is a disease characterized by low BMD and structural deterioration of bone tissue, which can lead to an increase in bone fractures. It mainly affects adults age 50 and older. The National Osteoporosis Foundation, or NOF, estimates that approximately nine million adults in the United States have osteoporosis and more than 43 million have low bone mass, placing them at increased risk for osteoporosis and broken bones. In addition, the NOF has estimated that osteoporosis is responsible for more than two million bone fractures in the United States per year resulting in an estimated $19 billion in costs.

Table of Contents

Index to Financial Statements

Two main types of osteoporosis drugs are currently available in the United States: anti-resorptive agents and anabolic agents. Anti-resorptive agents act to prevent bone loss by inhibiting the breakdown of bone, whereas anabolic agents stimulate bone formation to build new, high-quality bone. We believe that existing anti-resorptive therapies have shortcomings in efficacy, tolerability and convenience. In part due to these limitations, anabolic agents are generally used as an alternative to anti-resorptive agents. For example, bisphosphonates, the current standard of care and a type of anti-resorptive agent, do not stimulate new bone growth, and have been associated with infrequent but serious adverse events, such as osteonecrosis of the jaw (a bone disease where the jaw bone begins to weaken and die), atrial fibrillation, and anomalous bone fractures, especially of long bones, resulting from frozen bone (a condition that shuts down the body s natural process of bone breakdown and regeneration). We believe that this limitation on their efficacy and safety concerns related to these serious adverse events which may limit their duration of use, has created demand for bone anabolic agents as an alternative to anti-resorptive agents.

The only anabolic agent approved in the United States for the treatment of severe osteoporosis is teriparatide, which is marketed by Eli Lilly & Company, or Lilly, as Forteo®, which must be injected daily and is unstable at room temperature. Based on our 2010 osteoporosis market survey, we estimated that in 2010 only 6% of the treated population of severe osteoporosis patients in the United States received prescriptions for Forteo®. Nevertheless, worldwide sales of Forteo® in 2015 were approximately $1.35 billion. We believe there is significant opportunity for a convenient and easy to use alternative for osteoporosis patients.

Completed Daily ZP-PTH Phase 2 Clinical Development

In 2008, we completed a Phase 2 clinical trial of Daily ZP-PTH. The objective of the study was to determine the safety and efficacy of our microneedle patch system compared to a placebo patch and a subcutaneous teriparatide 20 µg injection in post-menopausal women with osteoporosis. The Daily ZP-PTH Phase 2 clinical trial demonstrated the fast-on, fast-off pharmacokinetic profile we believe is critical for strong anabolic effect, which we believe contributed to the increases in lumbar spine and hip BMD illustrated in the tables immediately below.

Table of Contents

Index to Financial Statements

In the tables above, the confidence interval, or CI, means a range of values for a variable of the measure of treatment effect, constructed so that this range has a specified probability of including the true value of the variable. P-value, or p, means the level of marginal significance within a statistical hypothesis test, representing the probability of the occurrence of a given event.

The pharmacokinetic profile for all patch doses showed a faster time to peak concentration and a shorter apparent half-life than the subcutaneous teriparatide 20 µg injection, as illustrated in the following tables:

In terms of safety, the mean serum calcium for all Daily ZP-PTH doses increased moderately, but remained within the normal range. None of the patients discontinued the trial due to hypercalcemia (which is an elevated level of calcium in the blood) or hypercalciuria (which is an elevated level of calcium in the urine), potentially dangerous conditions with cardiovascular risk. During the six months of therapy, there was no clinically significant, or outside the range of normal, hypercalcemia observed and there were no clinically significant changes in liver functions, renal functions, blood counts or electrocardiograms. Also, no antibodies against PTH were detected nor any skin infection observed in any of the Daily ZP-PTH treatment groups.

In summary, the Daily ZP-PTH Phase 2 trial demonstrated that transdermal delivery of PTH using our microneedle patch system increased bone density over six months, and demonstrated:

- a faster T_{MAX}, a higher C_{MAX} and a shorter half-life (critical to the efficacy of an anabolic) observed with the Daily ZP-PTH patch versus Forteo.® T_{MAX} is a measure of the time after administration of a drug when it reaches the highest serum concentration. C_{MAX} is a measure of the peak serum concentration achieved after the drug has been administered; and

- comparable efficacy compared to Forteo® as measured by both six-month spine BMD and six-month hip BMD, even with lower bioavailability versus Forteo®. Bioavailability is the degree and rate at which an administered dose of unchanged drug is absorbed into the body and reaches the blood.

Weekly ZP-PTH Phase 1 Clinical Study

During the fourth quarter of 2013, we commenced a Phase 1 clinical study in healthy post-menopausal women of a single application of one or two Weekly ZP-PTH transdermal patches coated with doses ranging from 60 µg to 160 µg of teriparatide, compared to subcutaneous injections of teriparatide at doses of 20 µg or 57 µg. The design was a single-center, open-label, randomized eight-way crossover study in 32 subjects. Test treatments included single patches of 60 µg, 120 µg, 160 µg doses, two patches of 60 µg (120 µg total PTH), two patches of 90 µg (180 µg total PTH), two patches of 120 µg (240 µg total PTH), and doses of two active injectable comparators: teriparatide 20 µg (Forteo®) by subcutaneous injection, and teriparatide 57 µg

Table of Contents

Index to Financial Statements

(Teribone) by subcutaneous injection. The rationale of the patch dose selection was driven by our desire to replicate the demonstrated efficacy of 28 µg and 57 µg subcutaneous injections in studies conducted by Asahi Kasei Pharma Corporation, or Asahi, while adjusting for a higher bio mass index in a Caucasian population.

As indicated by the chart below, showing mean results, the Phase 1 study demonstrated pulsatile performance with all patch doses, which we believe is a significant factor for anabolic efficacy.

Zosano Ph1: Assess Pulsatile Delivery and Adequate Bioavailability

with Patch Doses vs. Injectable (n=32)

The study results also demonstrated:

- The bioavailability of our selected patch doses bracketed the subcutaneous doses of 28 µg and 57 µg, which have proven to be efficacious in reducing fractures in Japanese patients. Our patches illustrated high bioavailability, dose proportionality in ascending doses in the single-patch systems, and dose proportionality in ascending doses in the two-patch systems, enabling us the flexibility of dose selection for future clinical studies; and

- With all weekly doses on one- or two-patch systems, we achieved the desired pulsatile pharmacokinetic profile which we believe is critical for anabolic efficacy. We observed pulsatile pharmacokinetic profile comparable to that in our Daily ZP-PTH Phase 2 study and in our 2008 005 ZP-PTH study.

Patch doses were similarly tolerated when compared to Forteo® and Teribone . The Phase 1 study was conducted in Australia and, as such, was not subject to an IND and was conducted in compliance with applicable Australian regulations.

We had a pre-IND meeting with the FDA, a meeting required for the filing of an investigational new drug application, or IND, in July 2014 to discuss the clinical study design for our Phase 2 and Phase 3 studies of Weekly ZP-PTH.

Table of Contents

Index to Financial Statements

Demonstrated 36-Month Stability of ZP-PTH Formulation

The stability of a drug formulation means the extent to which the formulation is able to maintain its physical and chemical properties over time under specified environmental storage conditions. In our internal studies, our Daily ZP-PTH formulation coated on the patch and stored at room temperature in its sealed, nitrogen-filled package retained over 98% of its purity for 12 months and over 97% of its purity after 36 months. By contrast, Forteo® retained less than 87% of its purity after 12 months when stored at room temperature, and less than 95% of its purity after 12 months when under refrigeration (2-8°C).

Strategic Alliance with Eli Lilly and Company

In November 2014, we entered into a collaboration agreement with Eli Lilly and Company, or Lilly, to develop a formulation of ZP-PTH to be administered daily using our microneedle patch system for the treatment of osteoporosis. Under the terms of the agreement, we granted to Lilly an exclusive, worldwide license to commercialize any ZP-PTH product using our microneedle patch system. We were responsible, at our own expense, for developing Daily ZP-PTH, including clinical, regulatory and manufacturing scale-up activities. Lilly would be responsible, pending successful clinical study outcomes and regulatory approval, for commercialization of our Daily ZP-PTH product. We had the right to terminate the agreement at any time prior to regulatory approval of Daily ZP-PTH in the United States or Japan if we determined that a critical success factor under the agreement was commercially or scientifically unreasonable to achieve and we discontinued development of Daily ZP-PTH.

In September 2015, we terminated the collaboration agreement in accordance with the terms following our determination that it was commercially unreasonable to pursue one of the critical success factors under the agreement, relating to the required timing of worldwide regulatory approval of Daily ZP-PTH by 2019.

As a result of the termination of the agreement, the exclusive, worldwide license that we granted to Lilly terminated and reverted to us, and we will no longer be eligible to receive any milestone or other payments from Lilly. If, prior to August 19, 2019, we decide to resume development of Daily ZP-PTH, then we will be required to notify Lilly and offer to reinstate the collaboration agreement on the same terms or on other mutually agreeable terms.

We also entered into a common stock purchase agreement with Lilly in November 2014 pursuant to which Lilly has purchased $15 million worth of our common stock in a private placement concurrent with the closing of our initial public offering of shares of our common stock, at a price per share equal to the initial public offering price. On January 30, 2015, concurrent with the closing of our initial public offering, we issued and sold 1,363,636 shares of our common stock to Lilly and received net proceeds of $14.5 million pursuant to the common stock purchase agreement. As of December 31, 2015, Lilly beneficially owned more than ten percent of our outstanding common stock.

ZP-Glucagon for Severe Hypoglycemia

Our product candidate ZP-Glucagon is our proprietary formulation of glucagon, a hormone that raises blood glucose levels, intended for the emergency rescue of patients suffering from life-threatening, severe hypoglycemia. Severe hypoglycemia is a complication of diabetes treatment, often caused by insulin overdose, characterized by a very low level of blood glucose that can lead to loss of consciousness, seizure, coma and death. Timely treatment is critical, and may need to be administered to an incapacitated patient in a life- threatening situation by a third party who lacks medical training. We believe that ZP-Glucagon delivered using our microneedle patch system will offer patients and caregivers a simple device providing rapid onset and enhanced ease of use, as well as extended room temperature

stability, compared with the two glucagon products currently marketed in the United States.

In January 2014 we completed a Phase 1 trial that demonstrated faster onset, a higher bioavailability and lower variability (which is the range of the data points from the trial showing the measure of the treatment s

Table of Contents

Index to Financial Statements

effect in relation to the mean of the data points) with ZP-Glucagon treatments compared to glucagon injection. The Phase 1 trial was conducted in Australia and, as such, was not subject to an IND and was conducted in compliance with applicable Australian regulations.

In October 2015 we announced positive Phase 2 clinical trial results on our ZP-Glucagon patch program for the treatment of severe hypoglycemia. The objective of our Phase 2 clinical trial in Australia was to evaluate the performance of our ZP-Glucagon patch in Type 1 diabetic patients at 0.5 milligram, or mg, and 1.0 mg doses, with induction of hypoglycemia, in comparison to comparable doses of glucagon administered by intramuscular injection. Both ZP-Glucagon patch doses normalized blood sugar in 100 percent of the subjects. Both patch doses had rapid onset of action and time to glucose response was similar among the two modes of administration. All treatments were well tolerated and no new safety issues were identified.

We believe that we have made significant progress in the clinical development of our ZP-Glucagon product candidate and intend to evaluate strategic opportunities with a corporate partner to further its clinical and commercial development.

Underserved Severe Hypoglycemia Market

Severe hypoglycemia is a life-threatening potential complication of diabetes treatment, for which timely treatment is critical. The current standard of care in a severe hypoglycemic event is administration of glucagon by injection or infusion. The treatment is typically provided by a third party, caregiver or a bystander, as the patient is typically unable to self-administer the drug. Despite the risks involved with hypoglycemia, many insulin-dependent patients do not carry glucagon rescue kits.

There are 21 million diagnosed diabetes patients in the United States, of whom 26% are insulin-dependent. Insulin-dependent patients have on average 1.2 severe hypoglycemic events per year. There are currently two glucagon products marketed in the United States: Glucagon Emergency Kit by Lilly and GlucaGen® by Novo Nordisk. Based on a market survey of the hypoglycemia market commissioned by us in 2013, we estimate that in 2012, sales of these products exceeded $120 million in the United States with units sold at an average wholesale price of $188 per unit, and that the injectable glucagon market is growing at approximately 15% year- over-year, largely driven by ongoing price increases.

The two glucagon products currently marketed in the United States for severe hypoglycemia are both injectables. Due to its chemical constitution, the glucagon molecule is inherently unstable, and both commercially available products require a multi-step reconstitution process prior to use. Reconstitution and injection are typically administered by a third party who may lack medical training.

Table of Contents

Index to Financial Statements

We believe that ZP-Glucagon delivered using our microneedle patch system will offer patients and caregivers the benefit of a simple, easy-to-use device with rapid onset, room temperature stability and enhanced portability, benefits that we believe will encourage patients to carry our product as a glucagon rescue kit.

We expect our finished product to be a single-use, disposable, pre-loaded microneedle patch system. We have designed our product to be intuitive and to be administered with a simple press-and-apply action without requiring any cumbersome reconstitution. We intend to introduce a Generation 1 product consisting of our existing 3 cm2 patch and a single use applicator.

The practical advantages afforded by the room-temperature stability of our microneedle patch system, eliminating the need for reconstitution and allowing for immediate administration, may be as important as the therapeutic benefits of rapid onset. We believe that our formulation of ZP-Glucagon, which we have demonstrated is stable for at least six months, will enable us to market ZP-Glucagon as a ready-to-use product. In our most recent stability studies with the formulations of glucagon that we plan to use in our future clinical trials (Formulation C and Formulation D), the formulations demonstrated purity levels in excess of 99% after six months at 40°C, or in excess of 100°F, a temperature significantly higher than room temperature, and consistent with the ambient temperatures that might be encountered in a warm climate by a patient carrying the product in a pocket or purse.

Completed Phase 1 Clinical Trial

In January 2014, we completed a Phase 1 trial of ZP-Glucagon designed to assess relative bioavailability with our microneedle patch system on a 3cm2 patch compared to GlucaGen® administered by intramuscular injection. We compared subjects across multiple application sites with two formulations (formulation C and formulation D) in a single-center, open-label, randomized five-way crossover study using 0.5 mg on both the ZP- Glucagon patch and GlucaGen®. The study included 20 healthy volunteer subjects.

Table of Contents

Index to Financial Statements

We achieved a faster onset and a higher bioavailability with each of the ZP-Glucagon treatments vs. the Glucagon intramuscular injection. The pharmacokinetic and pharmacodynamic data are shown in the graphs below. The table below the two graphs shows the data points in the first of the two graphs, and the CV, or coefficient of variation, which represents the variability of the specified data points.

Treatment	AUC last	AUC 30min	AUC 30min (% > IM)	T max (min)	C max (pg/mL)
Glucagon IM Upper arm	1558±685	1106±553		11.8±4.4	2333±1256
	CV 44%	CV 50%			
Patch C Upper arm	1921±551	1724±492	56%	6.9±2.4	5438±1754
	CV 29%	CV 29%			
Patch C Forearm	1669± 473	1441±395	30%	8.1±3.9	4136±1393
	CV 28%	CV 27%			
Patch C Abdomen	1988±769	1664±596	50%	8.4±3.4	4785±1791
	CV 39%	CV 36%			
Patch D Abdomen	1440±667	1270±580	15%	8.5±2.9	3918±2021
	CV 46%	CV 46%			

Note: AUC measured in ng*hr/mL

Completed Phase 2 Clinical Trial

In October 2015, we completed a Phase 2 clinical trial in Australia to evaluate the performance of our ZP-Glucagon product candidate in Type 1 diabetic patients at 0.5 mg and 1.0 mg doses, with induction of hypoglycemia, in comparison to comparable doses of glucagon administered by intramuscular injection, or IM.

The Phase 2 clinical trial investigated the safety and efficacy of ZP-Glucagon in the treatment of insulin- induced hypoglycemia in diabetic patients (as opposed to healthy volunteers, as used in our Phase 1 clinical trial). Based on the higher bioavailability results from our Phase 1 clinical trial, it is possible that we could have a therapeutic patch dose with a coated amount less than 1 mg. Therefore, in our Phase 2 trial, we were testing both a single patch dose of 0.5 mg and two patches of 0.5 mg (total dose of 1.0 mg) compared to 0.5 mg and 1.0 mg of intramuscular injection.

Our Phase 2 clinical trial was a four-way crossover study with 16 diabetic patients, each of whom was administered the following four doses:

One patch of ZP-Glucagon 0.5 mg applied on the upper a