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Relating to Registration Statement No. 333-196983

This free writing prospectus relates to the initial public offering of common stock of Zosano Pharma Corporation (the Company).

The Company has filed with the Securities and Exchange Commission (SEC) a registration statement on Form S-1 (No. 333-196983), including a preliminary prospectus (the Preliminary Prospectus), for the offering to which this communication relates. Before you invest, you should read the Preliminary Prospectus and other documents the Company has filed with the SEC for more complete information about the Company and the offering. You may obtain these documents for free by visiting EDGAR on the SEC website at http://www.sec.gov. Alternatively, copies of the Preliminary Prospectus may be obtained from Wedbush Securities Inc., Two Embarcadero Center, Suite 600, San Francisco, CA 94111, Attn: ECM Prospectus Department, by calling 415-274-6819 or by email at vinnie.devone@wedbush.com. You may obtain a copy of the Preliminary Prospectus at http://www.sec.gov/Archives/edgar/data/1587221/000119312514270452/0001193125-14-270452-index.htm

On July 26, 2014, Vikram Lamba, the Company s Chief Executive Officer, sent an email to a representative of a prospective investor responding to questions following an in-person road show meeting. The content of that email is set forth below. You should consider the statements contained below only after carefully evaluating all of the information in the Preliminary Prospectus.

* * *

Great meeting you too, [name omitted], and thanks for the time yesterday. We have been traveling extensively so far and didn t have a chance to get back immediately. Happy to answer your questions in more detail via a phone call if you would like to but have tried to summarize below as succinctly and comprehensively as possible:

1. The maximum active drug API payload that can be put on a patch depends on (1) the active molecule (2) the weight of the excipients in the formulation (some formulations have almost no excipients and others can have as much as 50%) and (3) the coatable surface area on the patch (we use $2cm^2$, $3cm^2$ and $6cm^2$ patches). The maximum amount of API on a $3cm^2$ patch that we showed you yesterday is approximately 2mg and the $6cm^2$ patch can load 4mg.

2. The ratio of bioavailability via patch versus SC depends on the molecule under discussion. For example, if you see the mean AUC data from our Phase 2 Daily PTH study on p96 of the prospectus, you will notice that the patch bioavailability relative to SC is approximately 42% for PTH. However, when you see similar comparative AUC data for Glucagon on p101 and the attached slides, the relative patch BA versus IM injection is approximately 150% in the first 30 minutes where the exposure is most critical. While these relative BA numbers may be different for different molecules, they are pretty consistent across multiple

patients and applications. Our CV s versus injectables are comparable and sometimes, even lower.

3. The data we showed you for the 6-month Phase 2 study (p95 and 96 of the prospectus) was an outpatient study with 165 patients who self-administered the patches every day. There are other studies where we have applied the patches in a controlled setting. The system is supplied as an intuitive and easy to use system that is easily managed by the patients in an out-patient setting.

   The most extensive inter-patient variability data is also the individual patient AUC scatter plot for the Daily PTH Phase 2 study on p96. Attached is our published date showing the lower variability of the self-administered ZP-PTH patch compared to FORTEO® injection. The coefficient of variation was 39% for FORTEO® and 34%, 33%, and 36% for the 20, 30, and 40 µg ZP-PTH patches, respectively. The data for Phase 1 ZP-glucagon are also very consistent in showing less variability than the injected marketed product (slides).

* * *

The following research paper, captioned Parathyroid Hormone (1-34)-Coated Microneedle Patch System: Clinical Pharmacokinetics and Pharmacodynamics for Treatment of Osteoporosis, was attached to Mr. Lamba s email.

Pharm Res
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RESEARCH PAPER

Parathyroid Hormone (1-34)-Coated Microneedle Patch System: Clinical Pharmacokinetics and Pharmacodynamics for Treatment of Osteoporosis

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ABSTRACT

Objectives To evaluate the clinical PK/PD of PTH(1-34) delivered by a novel transdermal drug-coated microneedle patch system (ZP-PTH) for the treatment of osteoporosis.

Methods Phase 1 PK studies evaluated the effect of site of administration, patch wear time and dose in normal volunteers, ages 40 85 yrs. Phase 2 was conducted in post-menopausal women with osteoporosis to determine the patch dose response compared to placebo patch and FORTEO® injection.

Results Phase 1 ZP-PTH patch delivery demonstrated a rapid PTH plasma pulse profile with T_{max} 3 times shorter and apparent $T_{1/2}$ 2 times shorter than FORTEO®. In Phase 2, ZP-PTH 20, 30 and 40 μg doses showed a proportional increase in plasma PTH AUC. Inter-subject and intra-subject AUC variability was similar for all patch doses and comparable to injection. All patch doses produced a significant increase in spine bone mineral density. Unexpectedly, ZP-PTH also produced an early increase in hip bone mineral density, an effect not observed with the injection.

Conclusions These studies suggest that this novel ZP-PTH patch system can deliver a consistent and therapeutically relevant PTH PK profile. Based on encouraging Phase 2 safety and efficacy data, the program is advancing into a pivotal Phase 3 clinical study.

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KEY WORDS Parathyroid hormone PTH (1-34) teriparatide osteoporosis transdermal microneedle patch pharmacokinetics pharmacodynamics Macroflux

INTRODUCTION

Several transdermal and intradermal technologies are in proof of concept and early product development for the needle-free delivery of therapeutic peptides, proteins, antibodies and vaccines. In all cases, advancement of these delivery technologies has been driven by specific product-development requirements, e.g. drug dose, stability, release rate and PK/PD for therapeutic effect of the drug and the need for a patient-friendly delivery system.

Zosano Pharma is developing products using a novel transdermal microneedle drug delivery system (formerly Macroflux®, ALZA Corp). The patch system incorporates a drug-coated titanium microneedle array and a hand-held, reusable applicator. The patch applicator system allows for the direct delivery of drug-coated microneedles into the superficial skin layers where the drug coating can rapidly dissolve, creating a local, high drug concentration to drive efficient systemic drug absorption. Previous clinical and preclinical studies have demonstrated the capability of this drug-coated microneedle patch technology to deliver peptides, recombinant proteins and vaccine antigen (1 6).

Our lead product candidate in development is ZP-PTH, a microneedle patch system coated with parathyroid hormone (1-34) for the treatment of osteoporosis. This microneedle patch could offer several potential product advantages including a patient-friendly alternative to an injection, a room-temperature-stable product, and, most importantly, a rapid and efficient delivery with only a short patch wear-time (minutes).

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FORTEO® is a once-daily subcutaneous injection of human parathyroid hormone (1-34) peptide (PTH). It is the only US-approved anabolic (bone building) therapy for the treatment of advanced osteoporosis in men and post-menopausal women. PTH is unique in its bone building effect and ability to promote bone strength and reduce long-term bone fracture risk relative to bisphosphonates (anti-resorptive agents) (7,8). Currently, the use of FORTEO® is limited by the requirement for injection and the need for product refrigeration. A patient-friendly alternative to this daily injection could improve patient compliance and, thereby, therapeutic outcome (9,10). Intermittent dosing is also important to the mechanism of PTH s anabolic action. PTH subcutaneous injection results in a plasma C_{max} in 30 min followed by elimination in 3 h (11). While C_{max} does not appear to influence PTH anabolic effect, duration of drug exposure does (12). Several modeling studies have supported the need for a brief pulse plasma PTH profile with fast on set and fast off kinetics (13 16). While many attempts have been made to create PTH analogs with shorter time to C_{max} and shorter plasma exposure time, none have been successful to date. In a preliminary clinical study, we demonstrated that a PTH-coated microneedle patch system had the potential to deliver PTH with a pulse PK profile (17). Additional Phase 1 studies led to a successful Phase 2 study demonstrating ZP-PTH to be safe and effective in increasing lumbar spine and total hip bone mineral density in post-menopausal women with osteoporosis (18). ZP-PTH is now entering into Phase 3 clinical studies.

In this report, we describe the clinical pharmacokinetic and pharmacodynamic characteristics of a PTH (1-34)-coated microprojection patch system in development for the treatment of osteoporosis.

MATERIALS AND METHODS

Synthetic human parathyroid hormone 1-34, teriparatide (PTH) was obtained from Bachem Americas (Torrance CA) with a purity of 99.5%. Titanium metal sheets (commercially pure Grade 2, 25 micron thick) were obtained from Hamilton Precision Metals (Lancaster, PA).

Titanium microprojection arrays were fabricated by photo/chemical etching and formed using a controlled manufacturing process (19).

The ZP-PTH patch system consists of a 2 cm^2 titanium microneedle array with 1,300 microneedles/2 cm^2 arranged in a close-packed hexagonal design. Microneedles have an arrow-head shape with a length of 190 microns, maximum width of 115 microns, shaft width of 60 microns and thickness of 25 microns. The microneedle array is attached to an adhesive patch (Medical Tape 1523, 3M, St Paul, MN) and held in a disposable retainer ring (polycarbonate, Jatco,

Union City, CA) (Fig. 1a). The tips of the microneedles are coated with PTH (1-34) and dried using a previously described dip-coating process (20 22). Scanning electron microscopy (SEM) shows the coating is localized to the tips of the arrow-head-shaped microneedles with good coating uniformity (Fig. 1b). The PTH-coated patch in retainer ring is packaged in an aluminum foil pouch (Mangar, New Britain, PA) with a 3 Å molecular sieve desiccant sachet (3.5 g Minipax, Multisorb, Buffalo, NY), purged with dry nitrogen and heat sealed. For clinical studies, ZP-PTH was manufactured under Good Manufacturing Practices.

The patch is applied with a hand-held, reusable applicator. The patch ring is attached to the applicator with a press fit (Fig. 2a). The self-actuating applicator is pressed on the skin (Fig. 2b), releasing the patch and applying it with a predetermined force of 0.2 joules/cm^2 delivered in <10millisec (Fig. 2c) (1 3,23).

FORTEO® injection pens (rhPTH 1-34, teriparatide, Eli Lilly, Indianapolis, IN) were purchased from a commercial source and stored and used per the manufacturer s instructions.

Clinical Studies

All clinical studies were carried out in accordance with the Declaration of Helsinki (1964). All subjects signed informed consent forms, and study conduct was assessed at all study centers by independent Institutional Review Boards.

Pharmacokinetic Data

Phase 1 studies were all single-center, open-label, randomized cross-over in healthy post menopausal women, ages 40 85 years. In a first study, patches coated with 30 µg PTH 1-34 (ZP-PTH 30) were applied to the lateral abdomen, upper forearm, or thigh and worn for 30 min. The approved commercial dose of FORTEO® (20 µg) was administered by subcutaneous injection at the thigh. In a follow-up Phase 1 study, patches coated with 40 µg (ZP-PTH 40) were applied to the lateral abdomen and worn for 30 min, and FORTEO® was injected in the abdomen. In both studies, 23 25 subjects were tested in a cross-over study design. There was a 1-week wash-out between dosing. Further studies compared delivery from patches coated with 30, 40, or 60 µg applied to the abdomen. For PK modeling, all Phase 1 study data were used from 106 women comprising 237 patch applications and 103 subcutaneous injections of FORTEO®.

A Phase 2 study was conducted with 165 post-menopausal women (ages 50 81, mean 64 years) with osteoporosis. This was a five-arm, randomized, multi-center trial. Subjects self-administered either a ZP-PTH patch, placebo patch or FORTEO® injection daily for 6 months. Patch wear-time was 30 min. Sparse PK sampling (4 samples/subject) for the

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Fig. 1 Transdermal microprojection patch delivery system **a.** ZP-PTH patch/retainer ring; The titanium microneedle array is 2 cm^2 in area and attached to a 5 cm^2 adhesive with backing. The adhesive is attached to a polycarbonate ring with 4 scored tabs. **b.** SEM of PTH (1-34)-coated microprojection array: A) distance between microneedles: 370microns; B) length from microneedle tip to base plate: 190 microns; C) shaft width: 60 microns. The PTH (1-34) formulation coating is restricted to the arrowhead area of the microneedle. The tip angle is 60 degrees and distance from tip to arrowhead base is 100 microns.

Phase 2 study was performed on 2 study visits (months 1 and 6) (18).

PTH (1-34) Plasma Assay

Blood samples were collected from subjects at base line at designated times after patch application and removal. Plasma PTH (1-34) was assayed using a previously described specific ELISA assay (24). The inter- and intra-assay variability were <4.8 and <7.7%, respectively. The lower limit of assay quantification was 11.3 pg/mL and was at least 5-fold over baseline.

Determination of Residual Patch PTH (1-34) After Patch Wear

After patch application and specified wear time, patches were removed and stored at 20°C. For residual PTH analysis,

patches were eluted with aqueous buffer and quantitated by HPLC.

Statistical Methods

Pharmacokinetic parameters, AUC_t, AUC_{inf}, C_{max},T_{max}, and $t_{1/2}$ were calculated for each treatment and subject in the Phase 1 studies using non-compartmental analyses.

The PK data of the Phase 1 and Phase 2 studies were also analyzed using a PK modeling approach. The data were analyzed using a subject-specific nonlinear regression model implemented in the NLME function in Splus 7.0 (Insightful Corp). The data were best described by a one-compartment disposition model with a biphasic slow and fast first-order absorption process for the ZP-PTH patch applications and a single first-order absorption process for the subcutaneous injections of FORTEO®. The model accounted for differences in bioavailability for formulation (injection *vs*. patch), application site (abdomen, thigh or arm) and application time. FORTEO® and the ZP-PTH patch were found to share the same disposition model (i.e. biological half-life) for PTH, and all differences between the two formulations were explained by differences in the absorption process. The model included random effects on the pharmacokinetic parameters by subject and by visit within subject. Subject-specific estimates of AUC and C_{max} were obtained for the subjects in the Phase 2 study and compared across the treatment arms.

All results are presented as mean +/ SD or mean +/ SEM. Statistical analysis was performed by analysis of variance (ANOVA). A probability value of p <0.05 was considered statistically.

RESULTS AND DISCUSSION

ZP-PTH System Stability

PTH stability studies on the packaged ZP-PTH showed retention of purity greater than 98% when stored at 25°C

Fig. 2 Patch application is a simple press and apply. **a.** the ZP-PTH patch in ring is attached to a hand-held, reusable applicator; **b.** the self-actuating applicator is pressed against the skin to release the patch from the ring; **c.** patch is applied at a pre-determined force of 0.2 joules delivered in <10 millisec.

for 2 years. Under accelerated stability conditions, 94% purity was retained at 40°C for 6 months. These data compare favorably to the stability of the commercial FORTEO® product stored as recommended at 2 8°C and demonstrate a stability improvement over the FORTEO® product stored at 25°C (Fig. 3). The stability of this packaged dry-coated microneedle patch system was dependent on the initial liquid coating formulation and coating conditions (21) but also on the final packaging (20), which excluded moisture (£5% RH) and oxygen (£1%).

PTH Delivery

ZP-PTH 30 μg applied and worn for 30 min on either the abdomen, upper arm or thigh showed a PTH PK profile with comparable T_{max} (Fig. 4). With all ZP-PTH treatments, T_{max} was 3 times shorter than with FORTEO® injection (0.14 h *versus* 0.4 h, respectively). The mean terminal half-life for PTH was ~2 times shorter with ZP-PTH application (0.5 to 0.8 h) than with FORTEO® (1.4 h) (Table I) Patch applied on the abdomen produced the most comparable relative exposure (~92%) to injection in the thigh but with higher C_{max} (~197%). Patch worn on the thigh achieved the most comparable C_{max} (~105%) to injection but with lower exposure (37%), while on the arm, the patch produced a higher C_{max} (~177%) but with lower exposure (56%) compared to injection and the patch applied to the abdomen (Table I).

Interestingly, the difference in relative drug exposure among the 3 patch application sites was not due to delivery efficiency from the patch into the skin site. Analysis of the patches and skin site after 30 min wear-time showed that

Fig. 3 Stability of packaged ZP-PTH compared to FORTEO® product.

Fig. 4 Phase 1 PK profile of PTH delivery by ZP-PTH 30 *μg* dose at 3 different application sites compared to FORTEO® 20 *μg* injection. n = 24 subjects with 4 way cross over study design.

the total amount of residual PTH was £20% from all skin sites, suggesting that absorption from the skin site may be different. It is not known whether this observation may be due to differences in site-specific microcirculation, drug metabolism, tissue binding or possibly other mechanisms.

Table II shows that the AUC of ZP-PTH 40 μg coated dose resulted in a relative exposure that was 77% of FORTEO® administered to the abdomen and was estimated to be the same (95 105%) as that of the injection administered to the thigh. The half-life for PTH administered by ZP-PTH 40 at the abdomen was 0.55 +/ 0.16 h compared to 0.88+/ 0.33 h with injection at the same site. The T_{max} for ZP-PTH 40 was shorter compared to FORTEO®, 0.12 h +/ 0.05 *vs*. 0.56 +/ 0.27 h, while the C_{max} was ~1.7 times higher. The plasma PK profile of patch-delivered PTH may be due to a faster input rate than the subcutaneous injectable. The initial delivery from the patch is very fast, and the fast decline in plasma concentrations after patch administration seems to be driven by the biological elimination half-life of PTH (about 0.2 h). Conversely, after subcutaneous injection, the absorption from the subcutaneous space seems to be rate limiting and determining the terminal decline in plasma concentration.

The effect of patch wear-time was evaluated for possible changes in plasma PTH T_{max}, C_{max}, and AUC. The PK analysis with patch wear-times of 30 min or 2 h showed no significant difference (Fig. 5). The T_{max} was 0.1 h in both

cases. The C_{max} was 207+/ 60 pg/mL and 228+/ 144 pg/mL and the AUC was 145+/ 27 pg-h/mL and 166+/ 56 pg-h-/mL for the respective 30 min and 2 h patch wear-times.

In Phase 2, our ZP-PTH patch system was shown to be safe and effective in 165 post-menopausal women with osteoporosis who are at high risk of bone fracture (18). The dose-ranging safety and efficacy study was multi-center, randomized, blinded, and placebo-patch-controlled, and FORTEO® was used as the active comparator. In this

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Table I Comparison of Phase 1 PK Parameters at 3 Different Application Sites

Parameter[a]	Treatment Mean±SD, *n* =24			
	ZP-PTH (1-34) 30 mcg			FORTEO® 20 mcg
	Thigh	Upper arm	Abdomen	Thigh
C_{max} (pg/mL)	56.9±27.8	96.4±63.8	106.9±39.6	54.3±21.8
T_{max} (h)	0.14±0.10	0.14±0.09	0.15±0.06	0.39±0.24
$t_{1/2}$ (h)	0.80±0.49	0.53±0.16	0.80±0.35	1.39±0.51
AUC_t (pg.h/mL)	29.9±24.0	46.5±35.9	65.7±38	81.7±38.9
Relative Bioavailability (%)	37.4±23.8	56.3±42.8	92.1±60.4	Reference
AUC_{inf} (pg.h/mL)	46.6±26.4	60.2±34.9	88.2±40.6	117.4±38.8
Relative Bioavailability (%)	40.3±20.1	51.7±27.1	81.5±46.3	Reference

[a] Presented using the calculation without dose normalization; AUC_t is 0 8h

5-arm study, subjects self-administered either ZP-PTH 20, 30 or 40 µg patch doses, placebo patch or FORTEO® injections daily for 6 months. The objectives were to evaluate for safety, pharmacodynamic effects and pharma-cokinetic profile of the administered doses.

The ZP-PTH patch delivered a dose-proportional plasma PTH pulse profile that was well described by the pharmacokinetic model based on all PK data (Fig. 6a). All patch doses showed a shorter time to peak concentration and a shorter apparent half-life than injectable PTH. The AUC was dose proportional, and there was no change in the AUC from the 1 month to the 6-month time point (last dose) (Fig. 6b). The AUC-ratio for ZP-PTH 40 µg compared to injection was 0.81 [0.68 to 0.98; 95%CI]. The AUC-ratios were 0.42 [0.35 to 0.50] and 0.63 [0.52 to 0.76] for the 20 and 30 µg patch doses. The between-subject variability in AUC was similar for ZP-PTH doses and injection. The coefficient of variation was 39% for

Table II Phase 1 PK Parameters of ZP-PTH 40 μg Compared to FORTEO® 20 μg Dose

Parameter[a]	Treatment Mean±SD	
	ZP-PTH (1-34) 40 mcg Abdomen (*n* = 25)	FORTEO® 20 mcg Abdomen (*n* = 23)
C_{max} (pg/mL)	133.7±50.8	78.4±28.2
T_{max} (h)	0.12±0.05	0.56±0.27
$t_{1/2}$ (h)	0.55±0.16	0.88±0.33
AUC_t (pg.h/mL)	78.6±29.9	105.4±36.0
AUC_t ratio (%)	77.6	Reference
AUC_{inf} (pg.h/mL)	93.8±27.1	125.4±35.0
AUC_{inf} ratio (%)	77	Reference

[a] Presented using the calculation without dose normalization; AUC_t is 0 8 h
FORTEO® and 34%, 33%, and 36% for the 20, 30, and 40 µg ZP-PTH patches, respectively. The coefficient of variation for the between-occasion variability within a subject was 24% for FORTEO® and 23%, 28%, and 30% for the 20, 30, and 40 µg ZP-PTH patches, respectively. The relative AUC of the ZP-PTH patch and injection in this study were similar to those observed in our previous Phase 1 studies. The geometric mean C_{max} ratio for ZP-PTH 40 µg (at 0.16 h)) compared to injection was 1.56 [1.31 to 1.85]. The C_{max} ratios were 0.82 [0.69 to 0.98] and 1.21 [1.01 to 1.45] for the 20 and 30 µg ZP-PTH doses. The CV% of between-subject and between-occasion within subject variability of C_{max} was in the same order and not different between FORTEO® and ZP-PTH patch. There was no effect of age, ethnicity or weight on dose exposure relative to that observed for the PTH injection.

After 6 months treatment, ZP-PTH patch produced a dose-proportional increase in lumbar spine bone mineral density of 3.0%, 3.5% and 5.0% for the 20, 30 and 40 µg groups, respectively, and compared well to the response from injection (Fig. 7a). The slope of the ZP-PTH patch bone mineral density gain to the AUC was 0.042+/-0.007

Fig. 5 Phase 1 PK profile of ZP-PTH 40 μg dose applied to the abdomen at 0.5 hr and 2 hr patch wear time. *N*=6 subjects per group.

Fig. 6 a. Phase 2 clinical comparison of PTH pharmacokinetics from ZP-PTH patch doses and FORTEO® injection. Symbols (¡), ZP-PTH 20, ( ), ZP-PTH 30, (p), ZP-PTH 40 and (¡), FORTEO® 20 μg injection are the mean PTH plasma concentrations at the indicated blood draw time points. The continuous lines represent the estimated PK profiles based on the PK model that also includes the data from the four Phase 1 PK studies; **b.** Phase 2 clinical comparison of the inter-subject PTH AUC with ZP-PTH doses and FORTEO®. Symbols (¡), ZP-PTH 20, ( ), ZP-PTH 30, (p), ZP-PTH 40 and (¡), FORTEO® 20 μg injection are each subject s AUC averaged from the 1 month and 6 month time points.

and was highly significant ($p< 0.001$). The ZP-PTH 40 dose showed a significant gain in lumbar spine bone mineral density despite having a lower relative exposure level (80%) compared to FORTEO®. Unexpectedly, the ZP-PTH 40 dose also shows a statistically significant increase in total hip bone mineral density at 6 months (1.3%, $p < 0.05$) over both placebo and FORTEO® injection (Fig. 7b). In other clinical trials, FORTEO® does produce a beneficial effect on hip bone mineral density; however, this effect is only observed after 1 year of daily treatment (7,25,26).

We hypothesize that the unique plasma profile of PTH delivered by ZP-PTH patch may explain the significant gains in bone mineral density response observed in the hip as well as the lumbar spine even with the lower relative dose exposure compared to FORTEO®. The higher peak concentration albeit with short duration and the shorter half-life of ZP-PTH delivery *versus* injection might be important in mediating this improved biological effect. Several clinical and preclinical studies (12 14) have

confirmed that a rapid rise in serum PTH (1-34) and a very short serum half-life and rapid fall-off is required for an anabolic rather than catabolic effect of this peptide. Clearly, the PK profile of plasma PTH plays a pivotal role in bone building (anabolic) and in bone remodeling. It is intriguing to consider that the more rapid pulse delivery of PTH using our ZP-PTH delivery system may further increase the therapeutic effectiveness of this drug over injectable administration. Further clinical study is warranted to support our hypothesis.

In this Phase 2 clinical study, the ZP-PTH doses were all judged as safe. Patch dosing was well tolerated, and there were no systemic adverse events different than FORTEO®. Patch site erythema was mild to moderate and transient. Over the 6-month out-patient daily patch application experience, there was no evidence of patch site skin infection or skin sensitization and no detection of a serum anti-PTH antibody response.

With these positive and encouraging data, ZP-PTH 40 is now moving into a pivotal Phase 3 clinical trial to gain more safety and efficacy data for a commercial product approval.

Fig. 7 Phase 2 clinical comparison of the percent gain in bone mineral density with ZP-PTH 20, 30 and 40 μg patch doses, placebo patch and 20 μg FORTEO® after 6 months daily treatment. **a.** Lumbar spine All ZP-PTH treatments were statistically greater than placebo, $p < 0.001$; **b.** Total hip- *ZP-PTH 40 shows a statistically greater response than placebo or FORTEO® injection, $p < 0.05$.

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CONCLUSIONS

The ZP-PTH patch system demonstrated ³2-year room-temperature stability. In Phase 1 and Phase 2 clinical studies, a consistent, rapid pulse delivery of PTH with a short duration of plasma exposure was observed with the microneedle patch system. The preferred skin application site was the lateral abdomen with a patch wear-time of 30 min. Delivery was unchanged with patch wear-time of 30 min up to 2 h. Our Phase 2 study showed the ZP-PTH patch was well-tolerated and shown to be safe and effective in post-menopausal women with osteoporosis. The patch showed a consistent dose response effect for AUC and C_{max}, and gains in bone mineral density at both the lumbar spine but also at the hip site. The PK profile of PTH delivery by the patch was consistent at the 1-month and 6-month (last dose) time points. There was no effect of age, ethnicity or weight compared to FORTEO®. PTH delivered by ZP-PTH may provide an ideal plasma profile that is even more beneficial to the anabolic drug effect. Further studies of this system are warranted.

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