# **ZS Pharma**

(ZSPH-NASDAQ)

Stock Rating: Outperform Industry Rating: Outperform

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# Late-Stage Solution to Unmet Medical Need; Initiating at Outperform

#### **Investment Thesis**

ZS Pharma is a development-stage specialty pharmaceutical company that is developing a promising treatment for hyperkalemia, or abnormally high levels of potassium in the bloodstream. Hyperkalemia is often caused by chronic kidney disease, diabetes, and heart failure. The data so far on ZS Pharma's lead program, ZS-9, is very impressive, with data showing 99% of patients reaching normal potassium levels within 48 hours. We believe ZS Pharma offers a potential game-changing opportunity in the hyperkalemia treatment market, a market currently undertreated largely because the current standard of care treatment, Kayexalate, has a poor profile. However, ZS-9 is not alone in looking to change the treatment of hyperkalemia, as another company, Relypsa, also has a drug for hyperkalemia in development. We believe that in the coming months, with the filing of ZS-9 in 1H15, excitement for ZS-9 will build and the market will better understand the large market opportunity for effective treatments for hyperkalemia.

#### **Forecasts & Valuation**

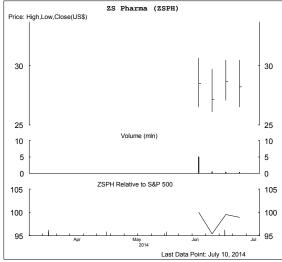
Our forecasts assume only a 12% market share by 2020, which we believe is very conservative. Based on extensive physician feedback, we believe ZS Pharma may have the edge with its drug, but our forecasts assume the two companies split the market. In this report, we reveal the results from two BMO Physician Surveys in which we provided data on both drugs to physicians. Approximately 54% preferred ZS-9 to Relypsa's drug. Physicians expect to use ZS-9 in approximately 50% of chronic kidney disease patients and heart failure patients who have hyperkalemia. We believe that ZS Pharma plans to go it alone in the US and partner in other territories, but may be a consolidation target if the data plays out as expected. Using a 15% discount rate and an 8x terminal multiple in our DCF, our price target is \$38. Discounting 2018 EPS by 15% and applying a 15x multiple, results in a \$34 price target.

#### Recommendation

We are initiating coverage of ZS Pharma with an Outperform rating and \$38 price target.

 Price (11-Jul)
 \$29.49
 52-Week High
 \$30.67

 Target Price
 \$38.00
 52-Week Low
 \$26.10



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(FY-Dec.)	2012A	2013A	2014E	2015E
EPS	- \$6.74	- \$21.84	- \$3.90	- \$3.10
P/E			na	na
CFPS	na	na	- \$4.20	- \$3.50
P/CFPS			na	na
Rev. (\$mm)	\$0	\$0	\$0	\$0
EV	na	na	\$558	\$558
EBITDA (\$mm)	-\$8	-\$32	-\$55	-\$73
EV/EBITDA	na	na	na	na
Quarterly EPS	Q1	Q2	Q3	Q4
2012A	na	na	na	na
2013A	na	na	na	na
2014E	-\$6.60	-\$0.93	-\$0.77	-\$0.78
Dividend	\$0.00	Yield		0.0%
Book Value	\$1.16	Price/Be	ook	25.4x
Shares O/S (mm)	18.7	Mkt. Ca	\$553	
Float O/S (mm)	na	Float Cap (mm)		
Wkly Vol (000s)	1,899	Wkly \$ '	Vol (mm)	\$54.0
Net Debt (\$mm)	na	Next Re	p. Date	na

Notes: All values in US\$

First Call Mean Estimates: Not available

## **Key Points**

ZS Pharma is a biopharmaceutical company focused on the development and commercialization of highly selective, non-absorbed drugs to treat renal, cardiovascular, liver, and metabolic diseases. Its lead program, ZS-9, is being developed for the treatment of acute and chronic hyperkalemia, or abnormally high levels of potassium. Hyperkalemia is often the result of one of several underlying conditions, including chronic kidney disease (CKD), diabetes, and chronic heart failure – diseases that have seen dramatic increases in incidence in recent years. ZS Pharma plans to target hyperkalemic patients being treated by cardiologists and nephrologists.

We believe ZS Pharma offers a potential game-changing opportunity in the hyperkalemia treatment market

**ZS** Pharma's **ZS-9** is in Phase III and expected to be filed for **US** approval in 1H2016. ZS-9 is an insoluble, non-absorbed zirconium silicate with a three dimensional crystalline lattice structure engineered to trap potassium ions. ZS-9 has a unique mechanism of action that enables high in-vitro binding capacity to potassium ions even in the presence of other ions.

**Major unmet medical need**. Hyperkalemia affects more than 44 million people in the US, and perhaps a similar number of people in Europe. The current standard of care is suboptimal.

**Very effective.** 99% of patients treated with ZS-9 (at 10 grams) were normokalemic in 48 hours. At the end of the 12-day maintenance period, 82% of patients who had received 10 grams once daily maintained potassium levels in the normal range.

**Rapid onset of action.** ZS-9 produced statistically significant reductions in potassium observed one hour after the first 10 gram dose of ZS-9.

In head-to-head in-vitro experiments, ZS-9 has demonstrated approximately ten times the potassium binding capacity of the current standard of care, sodium polystyrene sulfonate (SPS) or Kayexalate. Kayexalate is a nonselective polymer resin and polymer resins are less effective because they must traverse the entire gastrointestinal tract to reach the colon before having any significant impact on serum potassium. In the colon, a high concentration of potassium, mediated by aldosterone, out competes other cations such as calcium, magnesium, and sodium.

ZS-9 is expected to be administered orally at doses of 10 grams given three times daily to treat hyperkalemia and at 5 to 15 grams given once per day to prevent the reoccurrence of hyperkalemia.

#### Multiple value inflection points over next two- to three-year timeframe:

- Ongoing, started in June 2014: ZS005, open-label safety study to establish longterm safety and efficacy (n=500)
- o 3Q14: Commercial scale manufacturing
- Late 3Q/early 4Q14: Phase III ZS004 maintenance dosing clinical results
- o 1H15: NDA filing
- o 1H15: MAA filing
- July 2015: Initiate Phase I pediatric study (n=30) (not included in initial NDA/MAA)
- 4Q15-2Q16: NDA approval
- 2016: MAA approval

A late-stage asset for an unmet medical need with a limited physician target pool is very attractive, we believe, for in-licensing or acquisition by large pharma. We believe that interest is high from potential partners seeking international and even US rights to ZS-9, but perhaps the best time for ZS Pharma to determine the next best steps on the commercial side will be closer to the filing of the drug next year, when more will be known. In a nutshell, we think ZS Pharma is six months or a year from deciding whether to out-license ZS-9 in Japan, EU, and potentially in the US.

As a development-stage company with one lead program, there are many risks involved with investing in ZS Pharma, related to its pre-commercial stage, as well as other company-specific reasons. Investors should be aware of these risks, such as potential of clinical failure, manufacturing risks, and commercial execution risks, as well as others. Some of these risks are described later in this report.

We are initiating coverage with an Outperform rating and \$38 price target.

## A Market-Making Opportunity

We believe ZS Pharma's ZS-9, if approved, has the potential to greatly expand and radically alter the markets of several underlying conditions that lead to hyperkalemia, including chronic kidney disease, diabetes, and chronic heart failure markets. Hyperkalemia affects an estimated 44 million people in the US, and these patients typically suffer from chronic kidney disease (CKD), diabetes, and heart failure (HF). Cardiologists are often limited in their options to treat serious heart conditions with an otherwise effective renin-angiotensin-aldosterone system (RAAS) therapy, because the treatment also leads to hyperkalemia, and there are no efficacious medications on the market to treat hyperkalemia. ZS-9 could represent a significant commercial opportunity as physicians who otherwise would have limited or stopped a patient's RAASi therapy instead pair it with a potassium-binding medication like ZS-9.

Elevated potassium is usually detected with a lab test in a hospital setting or as part of treatment of another underlying disorder. Thus, the ideal drug will have few side effects and a rapid onset so that physicians can go about treating the underlying problem. That is, a patient with heart failure cannot afford to have the treatment of hyperkalemia negatively affecting the treatment of his heart failure.

If approved, we estimate ZS-9 would enter the market in 4Q16 – six months behind the company's planned launch in 1H16. ZS Pharma has plans to commercialize ZS-9 with an inhouse sales team in the US. ZS-9 addresses attractive markets that are large and focused, and will commercialize the drug to cardiologists and neurologists, who treat hyperkalemic patients.

#### Potassium in the Body

Potassium is an electrolyte that plays a very important role in the proper function of all cells, tissues, and organs in the human body. Further, potassium is crucial to heart function and plays a key role in skeletal and smooth muscle contraction, proving important for normal digestive and muscular function.

Normal serum potassium levels are maintained in the range of 3.5 to 5.0 mEq/L by hormones, including insulin, which shifts potassium into cells, and aldosterone, which stimulates the secretion of excess potassium through the kidneys and colon. Potassium is passively absorbed from a person's diet, while excretion is an active process through the kidneys. In response to fluctuations in dietary potassium intake, the body has developed methods to retain potassium when intake is low and increase potassium excretion when intake is high. In people considered to be healthy, kidneys excrete 90% to 95% of the absorbed potassium, while the remaining 5% to 10% is excreted in the colon.

The danger of having too much potassium in the blood is referred to as hyperkalemia and having too little is called hypokalemia. Elevated potassium levels can disrupt membrane activation in cardiac cells that regulate the electrical impulses that cause heart muscles to contract. Reduced contractions of the cardiac tissue can cause fatal heart arrhythmias, a main risk for patients with hyperkalemia.

#### **Possible Causes of Hyperkalemia**

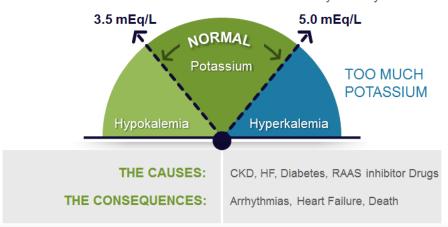
 Decreased excretion of potassium by the kidneys (common in patients with CKD and HF)

- Imbalances of potassium between the extracellular and intracellular fluid compartments (common in patients with diabetes)
- Use of several commonly used drugs that cause elevated potassium levels, including RAAS inhibitors, transplant medicines, and steroidal anti-inflammatory drugs

Older people are more at risk of hyperkalemia because their kidneys are less efficient at eliminating potassium as they age and are at risk when taking medications that may affect potassium levels, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and ACE inhibitors.

Exhibit 1: Potassium Balance Is Essential

PHYSIOLOGIC K<sup>+</sup> RANGE
Potassium Is Absorbed from GI Tract and Excreted by Kidneys and Colon



### **Objective**

To TREAT Hyperkalemia and MAINTAIN Normokalemia

Sources: Company presentation, BMO Capital Markets

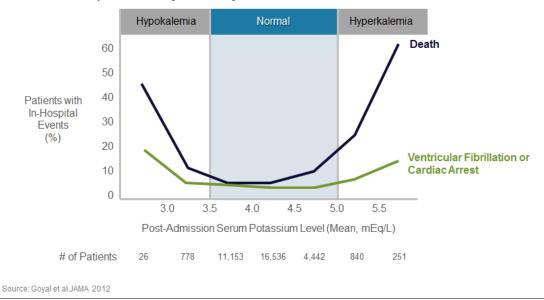
#### **Dangers of Hyperkalemia**

Hyperkalemia can lead to arrhythmias, heart failure and death, and the morbidity and mortality impact is significant. A patient can experience few symptoms until cardiac arrhythmia manifests resulting in hospitalization. Hyperkalemia is detected in approximately 1% to 10% of hospitalized patients and cardiac arrhythmias are the leading cause of mortality in hyperkalemia patients. Several studies published in the *Archives of Internal Medicine* and *Journal of American Medical Association* show the high correlation of high potassium levels with death and serious cardiac events. This, along with additional studies, points to evidence that reducing excess potassium levels in hyperkalemic patients reduces mortality risk.

**Exhibit 2: Serious Consequences of Uncontrolled Potassium** 

#### DEATH AND CARDIAC EVENTS INCREASE WITH POTASSIUM ≥ 4.5 mEg/L

#### Rates of In-Hospital Mortality/Morbidity

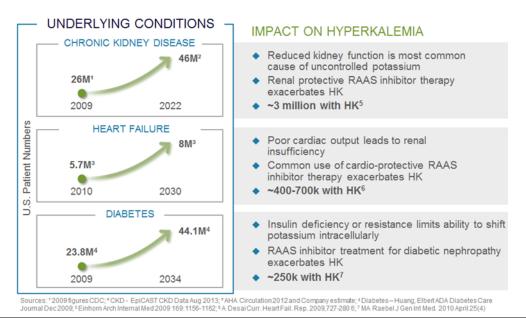


Sources: Company presentation, BMO Capital Markets

#### **Hyperkalemic Market**

Hyperkalemia occurs frequently in patients with CKD, HF, and diabetes. It is estimated that the number of patients in the US with CKD was 26 million in 2009 and is expected to reach 46 million by 2022. Further, the numbers of patients with heart failure and diabetes in 2009 were approximately 6 and 23 million, respectively, and are expected to continue to rise. According to industry sources, the prevalences of CKD and HF in Europe and Japan are similar to those in the US and growing rapidly. RAAS inhibitors, notably ACE inhibitors or angiotensin receptor blockers (ARBs), are the third most commonly prescribed class of medication in the US and are often used to treat patients with hypertension, HF, and CKD. Use of RAAS inhibitors can result in the retention of potassium in the kidney and increased serum potassium levels. Once these increased potassium levels occur, physicians are often forced to choose between the risk of hyperkalemia and the benefits of RAAS therapy.

**Exhibit 3: Hyperkalemia Is on the Rise** 



Sources: Company presentation, BMO Capital Markets

The number of patients suffering from CKD, HF, and diabetes is on the rise and without a safe and effective treatment option for hyperkalemia, the number of deaths and serious cardiac events resulting from hyperkalemia will increase as well.

#### **RAAS Inhibitors and Hyperkalemia**

The inhibition of the RAAS pathway reduces the hormone aldosterone, promoting potassium retention, leading to hyperkalemia. To regulate blood pressure in patients with hypertension, HF, CKD, and diabetes, doctors often use maximum doses of RAAS inhibitors which interrupt steps in the renin-angiotensin-aldosterone system (RAAS). Using these medications can decrease hospitalization, morbidity, and mortality in these patients. This predicament lays out a difficult decision for physicians to make – weighing the benefits of RAAS inhibitor therapy and the risk of hyperkalemia.

#### **Current Treatment of Hyperkalemia**

**ZS-9** is an effective and well-tolerated treatment that can rapidly lower and maintain normal potassium levels, proving it to be a superior treatment alternative to sodium polystyrene sulfonate (SPS). We believe ZS-9 could allow physicians to avoid reducing the use of RAAS inhibitor therapy for patients with hyperkalemia. The standard of care for the treatment of hyperkalemia varies depending on severity but falls into two groups: treatments that temporarily lower potassium by shifting it from extracellular to intracellular spaces and treatments that lower serum potassium by removing potassium from the body. The current standard of care is SPS, which was approved as a Drug Efficacy Study Implementation (DESI) drug in 1958.

The safety and efficacy of SPS has never been proven in randomized and controlled trials. SPS is a poorly tolerated drug with a high incidence of gastrointestinal (GI) side effects, including nausea, vomiting, constipation, intestinal necrosis, and diarrhea. The unpleasant side effects often lead to poor compliance that renders the drug unsuitable for chronic use.

**Exhibit 4: Current Treatment Options for Hyperkalemia** 

Diet	Sodium Polystyrene Sulfonate (SPS) or Kayexalate	Diuretics	Medication Avoidance
Avoid potassium rich or low sodium foods	30-90 g/day	Potassium Sparing	RAAS Inhibitors
<ul> <li>Limitations:</li> <li>Minimal efficacy</li> <li>Poor compliance</li> <li>Not long-term solution</li> <li>Removing foods that are otherwise healthy</li> </ul>	<ul> <li>Safety risk – FDA warning for colonic necrosis and other serious GI adverse events</li> <li>Unknown efficacy despite 56 years on the market</li> <li>Poor tolerance and adherence</li> </ul>	<ul> <li>Potential side effects</li> <li>May not be appropriate for all late-stage CKD patients</li> <li>Diuretic resistance</li> </ul>	Can cause blood potassium levels to rise     Optimal use limited by hyperkalemia     Potential side effects

Sources: Company presentation, BMO Capital Markets

#### Patients Don't Receive the Full Benefits of RAAS Therapy Due to Hyperkalemia

Many patients are not treated with RAAS inhibitor therapy or are undertreated because of the risk of hyperkalemia. Articles from the *American Heart Journal* and *European Heart Journal* showed that more than 50% of HF patients are on suboptimal RAAS inhibitor doses and up to 15% of HF patients are not on RAAS therapy at all. Over 70% of CKD patients with diabetes are not treated or are being treated below the recommended dose. From 2007 to 2010, the percentage of patients using ACE inhibitors or ARBs increased, but the number of patients with stage four or five CKD who were taking ACE inhibitors or ARBs declined compared with patients in earlier stages of the disease. We believe that ZS-9 has the ability to reduce the number of patients undergoing RAAS therapy who suffer from hyperkalemia, allowing for the full benefit of these medications to be realized. **ZS-9 could significantly alter the market, reduce the mortality rate, and slow the progression to end-stage renal disease.** 

#### **Superiority Over Existing Standard of Care**

In completed studies, ZS-9 showed approximately ten times the potassium binding of Kayexalate or SPS as well as some additional differentiating characteristics including:

- High efficacy in which 99% of patients from the completed clinical trials receiving a 10 gram dose returned to a normal level of potassium (between 3.5 and 5.0 mEq/L) in their blood or normokalemia within 48 hours;
- Rapid onset of action, with statistically significant reductions in potassium observed at one hour in patients receiving a 10-gram dose in completed clinical trials;
- Demonstrated ability in studies to date to safely and effectively maintain normokalemia, with a low risk of reducing the level of potassium in the blood below 3.5 mEq/L or hypokalemia;
- Potential suitability for chronic once-daily administration;
- Easily taken as a convenient oral suspension powder or dissolvable tablets;
- Shown to be well tolerated in studies to date, with an incidence of adverse events similar to placebo;
- Does not appear to have an effect on other electrolytes that are critical for normal physiological functioning, including sodium, calcium, and magnesium; and
- Stability at room temperature with a long shelf life, which has the potential to simplify distribution, physician sampling, and storage for both physicians and patients.

To date, ZS Pharma has observed that ZS-9 acts within hours of administration and daily administration maintains normal potassium levels for two weeks in its Phase III study.

#### **Targeted Patient Populations**

Patients suffering from CKD and HF are the major populations at risk for chronic hyperkalemia as a result of poor renal function and/or the need for treatment with RAAS inhibitors. ZS Pharma estimates there are over 30 million CKD and HF patients in the US and expects this number to grow to 50 million by 2022. ZS-9, if approved, will initially be marketed in the US to nephrologists and cardiologists who treat patients in one or more of the following categories:

- CKD patients with moderate to severe hyperkalemia;
- CKD and HF patients not taking a RAAS inhibitor or who have had their RAAS inhibitor dose reduced to address their hyperkalemia; and
- Patients with acute or episodic hyperkalemia

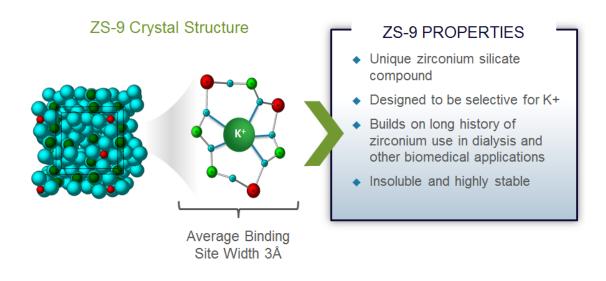
ZS Pharma believes there are additional opportunities in the US, including the treatment of patients in the US who are outside of the currently targeted specialty care market and for clinical needs outside the US.

### **ZS-9 Background and Data**

#### **Technology and Physical Properties**

ZS Pharma has proprietary zirconium silicate technology that creates highly selective ion traps, reducing toxic levels of specific electrolytes without disturbing the balance of other electrolytes. ZS Pharma licensed this technology from UOP, a division of Honeywell, and will owe UOP royalties equal to 5% of worldwide net sales, with a minimum of \$100,000, made by ZS Pharma. ZS-9 was designed to remove potassium in an effort to reduce serum potassium levels and treat hyperkalemia. This process involves a cubic lattice structure composed of pores. The ZS-9 compound consists of of zirconium, silicon, and oxygen atoms arranged to form ion binding pores that exchange hydrogen and sodium for potassium. The oxygen atoms in the crystal structure are positioned in a way that discourages the binding of other ions, including magnesium, calcium, and sodium. This allows the ion to specifically trap potassium despite the presence of other positive ions.

**Exhibit 5: ZS-9 Selectively Traps Potassium** 



Sources: Company presentation, BMO Capital Markets

ZS-9 is a non-absorbed, odorless, tasteless substance that has been formulated in both tablet and powder form.

A benefit of ZS-9 is its insolubility in typical solvents and ability to pass through the GI tract without degradation. In addition, it does not swell in water, so it can be eliminated from the body without the need for a laxative, which is often required with SPS. Another differentiating characteristic of ZS-9 compared with other competing products is that it does not require refrigeration or special handling.

Data thus far show ZS-9's higher selectivity for potassium, enabling it to absorb potassium immediately on ingestion and throughout the GI tract even when potassium is not the most

**plentiful ion.** To date, ZS Pharma has not observed any evidence of ZS-9 absorption in humans mainly due to its large diameter of approximately 20 to 30 micrometers.

#### The History of Zirconium

Zirconium has long been used in the medical field as a safe application for hip and knee implants, hemofiltration, hemodialysis, peritoneal dialysis, and wearable artificial kidneys. Zirconium-containing sorbent columns are being developed by Fresenius, a leading dialysis

provider, and zirconium containing sorbent columns have been used in over six million dialysis sessions for over 40 years without safety issues. Patients with CKD and little or no kidney function have their blood exposed directly to zirconium containing columns in sorbent hemodialysis sessions.

The amount of zirconium directly released into the blood of patients during each session has been quantified to be 0.758 mg (3,000 times a 10 gram dose of ZS-9). Further, zirconium is commonly found in quantities much higher than the amount of zirconium released from a 10-gram dose of ZS-9. These results, coupled with the non-absorbed nature of ZS-9, lead us to believe that ZS-9 will be well tolerated and safe in humans.

**Exhibit 6: Relative Zirconium Levels** 

Product	Amount	Relative to ZS-9
85 gram Antiperspirant Stick	2,295 mg	8,196,429x
Soil	300 mg/L	1,071,429x
Human Body Content	300 mg	1,071,429x
Daily Food Content	3.65 mg	13,036x
Zirconium from 4 Hour Sorbent Hemodialysis	0.758 mg	2,707x
Daily Drinking Water Content	0.65 mg	2,321x
Sea Water	0.004 mg/L	14x
Soluble Zirconium from 10 grams of ZS-9*	0.00028 mg	1.0x

<sup>\*</sup> Amount of zirconium in solution after exposing to simulated gastric and simulated intestinal fluids for a period of 24 hours.

Sources: Company presentation, BMO Capital Markets

#### Strong Clinical Data for ZS-9 So Far

ZS Pharma's clinical program has enrolled a hyperkalemic population, including patients with CKD, HF, diabetes, and those on renin-angiotensin aldosterone system, or RAAS, inhibitor therapy. Upon completion of long-term safety study, ZS005, approximately 1,500 patients will have been exposed to ZS-9.

**Exhibit 7: ZS-9 Development Overview** 

Trial	Trial Type	Patient Population	Duration	Objective	Summary
ZS002 (Completed)	Double-blind RCT Phase II	N=90 Hyperkalemia, CKD 5.0–6.0 mEq/L	48 hours	POC for ZS-9 rapidly lowering K* levels	Met primary endpoint
ZS003 (Completed)	Double-blind RCT Phase III	N=753 Hyperkalemia regardless of etiology 5.0–6.5 mEq/L	14 days	Confirm rapid K+ control and POC for maintenance dosing	Met primary endpoint for the 2.5g, 5g and 10g doses, and met secondary endpoint for 5g and 10g doses in maintenance phase
ZS004/e (Ongoing)	Double-blind RCT Phase III	N=230 Hyperkalemia regardless of etiology >5.0 mEq/L	1 Month + Extension	Establish a maintenance dose	Ongoing; results expected in Q4 '14
ZS005 (Ongoing)	Open label safety study	N=500 Hyperkalemia regardless of etiology >5.0 mEq/L	Up to 12 months	Establish long-term safety and efficacy	Started enrollment in Q2 '14

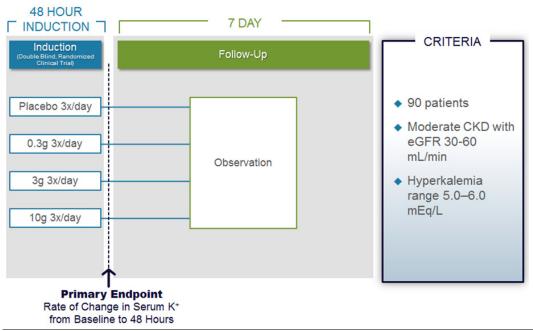
Sources: Company presentation, BMO Capital Markets

#### **Completed Studies**

ZS Pharma has completed clinical studies in 843 patients.

In the Phase II study, 100% of patients receiving the 10-gram dose had potassium levels less than 5.0 mEq/L and approximately 88% had levels less than or equal to 4.5 mEq/L within 38 hours. ZS002, which began in November 2011 and was completed in May 2012, was a dose-escalating, double-blind, randomized, placebo-controlled Phase II study in 90 hyperkalemic patients with CKD, including those on RAAS inhibitor therapy. This study aimed to determine ZS-9's ability to rapidly treat hyperkalemia. It met its primary endpoint, the rate of change in serum potassium over 48 hours.

Exhibit 8: ZS002 Study Design

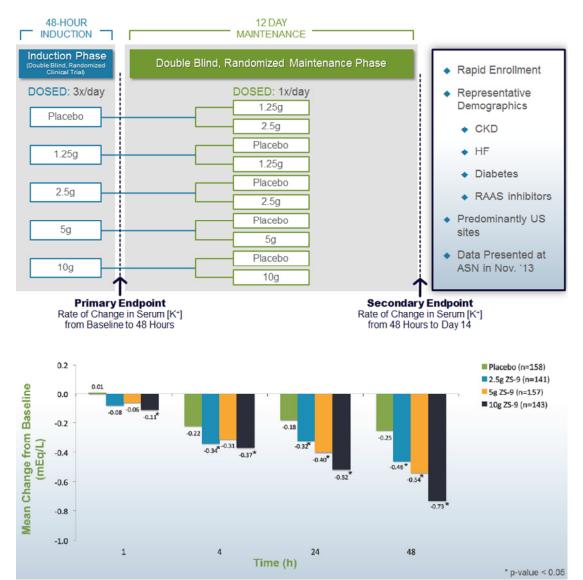


Sources: Company presentation, BMO Capital Markets

as used in ZS002, the rate of change in serum potassium over the 48-hour induction phase. ZS003 was initiated to confirm the acute findings found in ZS002 and explore ZS-9's ability to maintain normal levels of potassium for an extended period, regardless of etiology. The Phase III study was a two-part double-blind, randomized, placebo-controlled Phase III study in a representative population of 753 hyperkalemic patients including those with CKD, HF, and diabetes and those on RAAS therapy. Comparable to Phase II, statistically significant reductions in potassium were observed one hour after the first 10-gram dose of ZS-9. At the 10-gram dose, 99% of patients were normokalemic within 48 hours.

The Phase III study met its primary endpoint for the induction phase, which was the same

Exhibit 9: ZS003 Phase III Study Design and Reduction of Potassium



Sources: Company presentation, BMO Capital Markets

**ZS-9 was found to be efficacious across all patient subsets.** Patients with CKD, HF, and diabetes and those undergoing RAAS therapy all received the same magnitude of potassium lowering, approximately 0.6 mEq/L, as the entire intent to treat (ITT) population. In contrast, patients who had a higher potassium level to start with had a greater response to ZS-9, with an average decrease of 1.1 mEq/L.

Exhibit 10: ZS003 Showed Consistent Reduction of Potassium in All Patient Subgroups

	Placebo	1.25g	2.5g	5.0g	10.0g
Overall ITT Populations	-0.25	-0.30	-0.46	-0.54	-0.73
Disease Subsets (n; %)					
CKD (463; 61.5%)	-0.22	-0.31	-0.43	-0.58	-0.83
HF (300; 39.8%)	-0.24	-0.27	-0.46	-0.52	-0.78
RAAS inhibitors (491; 65.2%)	-0.24	-0.28	-0.48	-0.53	-0.73
Diabetes (451; 60%)	-0.25	-0.25	-0.47	-0.52	-0.74
Starting Serum K+					
Baseline S-K < 5.3 (n=427)	-0.15	-0.23	-0.39	-0.39	-0.57
Baseline S-K 5.4-5.5 (n=152)	-0.37	-0.37	-0.49	-0.65	-0.99
Baseline S-K > 5.5 (n=174)	-0.42	-0.34	-0.55	-0.87	-1.10

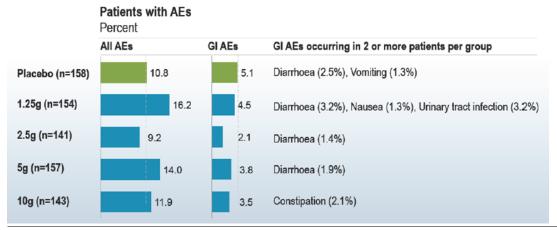
Sources: Company presentation, BMO Capital Markets

The results from the maintenance part of the study met the predefined efficacy points at the 5- and 10-gram doses. 82% of patients who received the 10-gram dose once daily maintained potassium levels in the normal range. Patients that became normokalemic after receiving ZS-9 in the induction phase were re-randomized to receive once-daily ZS-9 at the same dose level they had received three times daily during the induction phase or once-daily placebo. At this point, when ZS-9 was no longer administered, average potassium levels increased to near baseline levels, similar to those patients who received placebo during the maintenance portion.

In the induction and maintenance phases, hypokalemia (serum potassium level below 3.5 mEq/L) occurred in two patients, or 0.3% of all enrolled patients. These findings allude to ZS-9 working in conjunction with normal potassium excretion mechanisms to remove potassium when it is above 5.0 mEq/L, but when potassium drops below 5.0 mEq/L; the body lowers physiologic excretion to avoid hypokalemia. This may explain why hypokalemia has been rare within the dose range administered despite ZS-9's rapid and potent ability to remove potassium. In both cases, the hypokalemia was mild (3.1 and 3.4 mEq/L) and temporary and did not require any treatment.

There is a high rate of GI adverse events observed with SPS; however, ZS-9 appeared to be meaningfully better with the incidence of adverse events similar to those on placebo. There were a total of 16 serious adverse events reported in ZS003. These events were assessed by the study investigators and ZS Pharma - 15 were proven to be unrelated to ZS-9 and were well distributed between ZS-9 and placebo. Only one serious adverse event, gastroenteritis, was classified as possibly related to ZS-9; however, when unblended, this event was found to have occurred in a patient treated with placebo.

Exhibit 11: ZS-9 Has Similar Adverse Events Profile to Placebo



Source: Company Presentation, BMO Capital Markets

#### **Ongoing and Completed Studies**

**ZS** Pharma initiated a second Phase III study, **ZS004**, in March 2014, with data expected in the fourth quarter of 2014. ZS004 will explore the effectiveness of maintaining normal potassium levels during three months of therapy. The primary endpoint is a comparison of the average serum potassium levels in the ZS-9 and placebo groups. After completing the four-week randomized withdrawal phase, patients will be eligible to continue receiving ZS-9 for an additional two months in an open label extension phase. This study is ongoing, and there have been no serious adverse events reported related to ZS-9 to date.

Exhibit 12: ZS004 Phase III Study Design

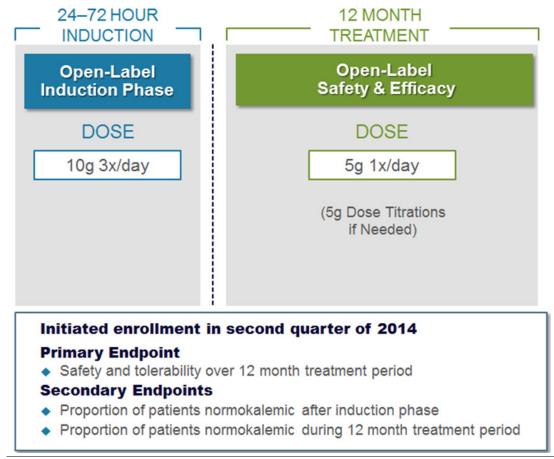


Sources: Company presentation, BMO Capital Markets

In the second quarter of 2014, ZS Pharma initiated enrollment for a long-term safety study, ZS005, to establish long-term safety and efficacy data by extending exposure to 52 weeks.

The primary goal of the 12-month portion of the study will be to demonstrate safety and tolerability of ZS-9, and the secondary endpoint will be control of serum potassium levels. ZS Pharma has submitted suggested protocols to the FDA and received guidance from the FDA on protocols for the development of ZS005. The FDA may provide additional guidance or change its guidance as ZS-9 moves through development, which is common.

Exhibit 13: ZS005 Study Design



Sources: Company presentation, BMO Capital Markets

ZS Pharma is on target to meet its NDA and MAA submission target in the first half of 2015 and launch in the first half of 2016. ZS Pharma intends to include safety data and efficacy data, if available, from the long-term study ZS005 as part of its submission package.

#### Nonclinical and Toxicology Studies

Nonclinical pharmacology studies have shown that ZS-9 binds potassium in solution and complex environments, for example in-vivo animal models. ZS-9 was not genotoxic and not associated with adverse events in cardiovascular, central nervous system, or gastrointestinal motility safety pharmacology studies. Single-dose in-vivo recovery studies in rats showed that ZS-9 is excreted in feces and is not systematically absorbed. Single-dose and multi-dose rat absorption studies are under way, and we believe ZS Pharma will have results in the third quarter of 2014. The company is also conducting additional nonclinical drug-to-drug interaction studies and long-term chronic exposure toxicology studies with ZS-9.

#### **Favorable Tolerability Profile**

Daily administration of ZS-9 has been observed to lower, and maintain control of, serum potassium levels, and thus far uphold a favorable tolerability profile. In the acute portion of the pivotal Phase III trial, ZS-9 showed statistically significant reductions in serum potassium, with 99% of subjects becoming normokalemic after receiving 10 grams of ZS-9 three times a day for 48 hours. In the extended portion of the trial, reductions achieved in the acute phase could be maintained using 5 grams or 10 grams of ZS-9 administered once daily. These results were also statistically significant when compared with patients randomized to placebo who had their potassium level revert to near pre-treatment levels. The Phase II study, ZS002, also showed statistically significant reductions in serum potassium levels, with 100% of patients becoming normokalemic after receiving 10 grams of ZS-9 given three times a day for 48 hours.

#### **Good Safety Profile**

**ZS-9** was observed to have a favorable safety profile and was well tolerated across the trial populations in the clinical program. In the completed trials, the most common adverse events were mild to moderate GI side effects, including nausea, vomiting, constipation, and diarrhea. However, these events occurred at similar rates and severity to patients receiving placebo, and no serious adverse events were found with ZS-9. We believe this shows the superiority of ZS-9's safety profile since product labels of approved potassium-binding treatment options, such as SPS, include warnings of severe GI side effects including GI necrosis, bleeding, and perforation, which can be fatal.

ZS Pharma believes the NDA and MAA will include the results from the Phase II trial (ZS002), Phase III trial (ZS003) and the ongoing Phase III one month randomized withdrawal study (ZS004). Approximately 1,500 patients will have been exposed to ZS-9 if all of the planned studies are completed.

#### **Pricing and Commercialization**

As ZS-9 has the potential to prevent hospitalizations and other expenses including the cost of dialysis, we believe ZS Pharma may be able to justify a premium price. However, we believe that ZS Pharma and Relypsa will likely price their drugs competitively. ZS Pharma plans to target a net price of approximately \$550 for ZS-9, slightly below the specialty threshold of \$600. We believe this price will likely be on par with that of Relypsa's Patiromer, although a price has not been disclosed, as well as many existing drugs with similar characteristics.

ZS Pharma intends to use its own specialty sales force to target approximately 5,000 nephrologists and 15,000 cardiologists and commercialize ZS-9 for the treatment of hyperkalemia in the US. ZS Pharma plans to seek partners for commercialization outside of the US that can sell ZS-9 in target markets and be structured to provide ZS the opportunity to receive milestones or other one-time payments in addition to royalties from product sales. Based on our discussions with management, we believe there are ongoing conversations relating to the commercialization strategy outside the US, and we do not anticipate any partnership agreements to be put into place prior to the filing of the NDA and MAA.

#### Competition

We believe that Relypsa (RLYP) will be ZS Pharma's top competitor, if both company's products are approved. Relypsa has a Phase III potassium removal drug, Patiromer, targeting the treatment of hyperkalemia.

According to our physician feedback from surveys and discussions, physicians seem to think that ZS-9 has an edge over Patiromer, although this is not overwhelming at this point. That said, Relypsa does have a head start in the approval process. Net-net, we do not think this is a winner-takes-all market, but rather that the hyperkalemic market is large enough to support both products. In our view, even if market share is split 50/50, both companies could realize significant commercial opportunities. Both Kayexalate and Relypsa's Patiromer are polymer-based treatments. Several doctors have noted that polymers, in theory, have more potential for GI issues compared with zirconium silicate. We believe that ZS-9's ability to target specific electrolytes without disturbing the balance of other electrolytes is a key advantage. Where Relypsa may have its own advantage is that it has a head start and is further along in completing clinical trials.

In the end, if both products are approved, the actual labels and marketed claims, side effect profiles, and formulary coverage may have a large impact on market share.

During the process of researching this report, we held several calls with the Relypsa management team to get their perspective of the marketplace, its drug, and potential areas of differentiation between their approach and competitors, such as ZS Pharma. We must first say that the Relypsa management team was exceptionally helpful, professional, and constructive about the marketplace and its clinical trial design. Sometimes in a competitive market with limited numbers of players, the debate becomes "who will win?" rather than "how big is the market?" and the discussion can become acrimonious among the players. We did not find that to be the case at all.

Overall, we believe that Relypsa sees that it has several strengths as it approached commercialization, including solid clinical data, an existing SPA with the FDA, redundant outsourced manufacturing, and a large safety database. We do not disagree with Relypsa's assessment of isixts strengths and believe that it has a viable product that will likely enter the market approximately 6 months ahead of ZS Pharma.

That said, we prefer the clinical profile of ZS-9 at this point, especially the fast onset of effect and suspect ZS will have a fair amount of patients for its longer-term safety data by the time of approval.

# Exhibit 14: ZS Pharma vs. Relypsa

Company	ZS Pharma	Relypsa
Product	ZS-9	Patiromer
Technology	Non-absorbed zirconium silicate with a defined three dimensional crystalline lattice designed and engineered to preferentially trap potassium ions throughout the GI tract	Non-absorbed, potassium-binding polymer, designed for the binding and removal of potassium from the GI tract, particularly the colon
Phase of	Initial Phase III completed, additional Phase III, open label	Phase III completed, no further trials planned
Development  Number of Studies	safety study & pediatric Phase I & Phase II/III studies planned Completed: 2 At filing/approval: 5	Current and at approval: 5
Primary Endpoints	Completed Phase III: The rate of change in serum potassium from baseline in both the 48 hour induction phase and the 12-day dosing period. Ongoing Phase III: comparison of the average serum potassium levels in the ZS-9 and placebo group	Reduction in serum potassium level at four weeks compared with baseline; the proportion of subjects requiring any dose modification of RAASi therapies (i.e. down titration or discontinuation) because of hyperkalemia at any time during the Part B 8-week period; the proportion of subjects receiving any dose of a RAASi medication at the end of Part B.
Recent Results	99% of patients in 10g dose normokalemic within 48 hours. At the end of the maintenance period, 82% of patients who had received 10 grams of ZS-9 once daily maintained serum potassium levels in the normal range. Patients who received 5 grams of ZS-9 once daily during the maintenance portion had an increase of 0.11 mEq/L compared to a placebo increase of serum potassium levels of 0.25 mEq/L and maintained normokalemia.	76% of patients has serum K+ in the target range (3.8 to 5.1 mEg/L) at week 4, and significantly more placebo patients required dose modification of their RAASi therapies (62%) than patiromer patients (6%), p < 0.001; with more patiromer patients (94%) still on RAASi medication at the end of the trial than placebo patients (48%), p < 0.001. The difference between the placebo and the patiromer groups in the median change from Part B baseline in serum potassium was 0.72 mEq/L (95% CI 0.46, 0.97), p < 0.001.
Onset-of-action	Statistically significant reductions in potassium were observed one hour after the first 10 gram dose of ZS-9	Statistically significant reduction from baseline in serum potassium levels was demonstrated at 7 hours after first 8.4 g dose and was maintained at all subsequent evaluations out to 48 hours (approximately 14 hours after the last dose)
Duration Studied	Current: 14 days At Filing: 6 months (< 100 patients) At Approval: 12 months (~150 patients)	Current and at filing: 12 months (~194 patients)
Manufacturing	Manufacturing and supplying their own API from two facilities, one in Coppell, TX, and one in Denver, CO. Guiding for 2015 commercial validation and launch quantities build out.	Current supplier of drug substance, Lanxess, only supplier in NDA but secured agreement with DSM Fine Chemicals and will file NDA supplement for approval. Both suppliers are well known and have made it through FDA before.
Estimated Timing of Filing	1H 2015 FDA & EMA	3Q 2014
Estimated Timing of Launch	1H 2016 (BMO Estimates 4Q 2016)	Late 2015
Potential Labeling Likely Dosing	Treatment of chronic and acute hyperkalemia  Orally at doses of 10 grams given three times per day intially to treat hyperkalemia and at doses of 5 to 15 grams given once per day to prevent the reoccurrence of hyperkalemia	Treatment of chronic and acute hyperkalemia  Orally twice a day at daily doses ranging from 8.4 grams to 50.4 grams
Intellectual Property Protection	Granted patents expire in 2019, regulatory exclusivity and the 30 month stay would effectively stop competition until 2023-2024. Filed patents, if granted, will expire 2032-2033.	Issued patents are expected to last until at least 2030
Side Effects	Most common adverse events were mild-to-moderate GI symptoms (3.5% for the 10g dose of ZS-9 given three times daily, compared to placebo rate of 5% in ZS003) including nausea, vomiting, constipation and diarrhea. These events occurred at a similar rate and severity as placebo treated patients. No serious adverse events were deemed attributable to ZS-9.	Adverse events potentially related to patiromer have primarily been mild-to-moderate GI symptoms in approximately 2 to 10% of subjects, including constipation, diarrhea, nausea and vomiting, as well as small reductions in serum magnesium levels (Source: Relypsa S-1). No serious adverse events were deemed attributable to Patiromer.

Sources: Company presentation, BMO Capital Markets

#### Manufacturing

In our view, the in-house manufacturing is both advantage and a risk to ZS Pharma. We believe the in-house manufacturing will better ensure the company's ability to meet market demand and allow it to achieve attractive cost of goods if ZS-9 is approved. ZS Pharma intends to manufacture the key components of ZS-9, but use outsourced packaging companies to complete the process. The drug's key ingredients, or API, is expected to continue to be manufactured in two manufacturing sites to establish a more diverse and volume-appropriate supply. The resulting material will be sent to finished product manufacturers to be processed and completed.

ZS Pharma's current capacity is not sufficient to produce quantities for launch; however, ZS is increasing production capacity. We expect ZS Pharma will enter into a long-term agreement with Sharp, the current packaging and drug product formation partner, or another drug product producer once approved by the FDA. We believe the reliance on more than one manufacturer will reduce supply risk.

ZS manufactures ZS-9 in-house in two facilities located in Coppell, Texas, and Denver, Colorado. The ZS-9 compound uses readily available starting materials (silicate solution, zirconium acetate, and sodium hydroxide) and requires a proprietary two-step manufacturing process. The result is a room temperature stable, dry, odorless powder that can be filled into packets or bottles or pressed into a dissolvable tablet and is easily suspendable in small amounts of water. There are 36-month stability studies ongoing that are expected to provide 24 months of data to support the NDA filing, which ZS Pharma expected will support the storage of ZS-9 for 36 months at 25 degrees Celsius. In addition, ZS-9 tablets are also being tested and are expected to support the storage for 24 to 36 months at 25 degrees Celsius.

ZS Pharma has completed the manufacturing of a 500-liter reactor for registration batches of ZS-9, which are being used for the pivotal Phase III trial and ongoing stability studies.

The next manufacturing campaign is expected to involve validation lots at the anticipated commercial scale. The commercial scale reactor is expected to be 2,000 liters, and ZS Pharma is evaluating the eventual use of a 5,000-liter reactor. Development of most analytical methods for impurities and commercial release testing has been completed, and is now being validated. The company has completed testing for impurities in drug substance registration stability batches and clinical batches using analytical procedures developed in-house and has found high purity of the drug substance. ZS Pharma believes the levels of impurities are below the suggested guidance recommendations. The control of impurities during API and drug product manufacturing will be confirmed through process validation, and ZS Pharma is using the maximum daily dose to establish the allowable levels of genotoxic impurities, impurities of special toxicological concern, and residual solvents.

We believe that the cost to build out the manufacturing footprint will be approximately \$70-80 million through 2018, but it could increase if management decides to expand use of the 2,000-liter reactor instead of developing the 5,000-liter reactor.

Exhibit 15: BMO Estimate for ZS Pharma's CAPEX (\$ in millions)

	2014	2015	2016	2017	2018	2019	2020
BMO Estimate for CAPEX	\$12	\$16	\$16	\$15	\$15	\$15	\$15

Source: BMO Capital Markets sstimates

ZS Pharma is expanding manufacturing capacity to support anticipated commercial scale quantities. ZS-9 is also being developed as an enema formulation for pediatric and hospital use.

#### **Potential for Cost of Goods Savings**

We believe ZS Pharma will have attractive margins at launch and are likely to improve margins as scale increases. ZS Pharma is manufacturing with a 500-liter reactor with an API cost of \$0.20/g which is expected to drop to \$0.08/g upon completion of the anticipated 2,000 liter reactor in mid-2014. If a 5,000-liter reactor is constructed and put into production, the API cost could be reduced to \$0.05/g. We believe this allows for very attractive margins and provides flexibility that would not be realized if it had to rely on a manufacturing partner.

#### **Existing Patents Under License**

ZS Pharma has patents under license from UOP, a division of Honeywell, including claims for compositions and methods for oral administration of ZS-9. If approved, ZS Pharma intends to list patents licensed from UOP in the Orange Book, including two composition of matter patents that, if the appropriate maintenance fees are paid, are expected to expire in 2017, and a method of treatment patent that, if the appropriate maintenance fees are paid, is expected to expire in 2019.

The UOP license grants worldwide rights; however, UOP does not have any issued patents or pending patent applications outside the US that are subject to the license agreement. ZS Pharma filed several nonprovisional and provisional patent applications directed to improvements and other novel zirconium silicate compositions, methods of treating various indications with ZS-9, and methods of manufacturing ZS-9. ZS Pharma recently received Notices of Allowances from the US Patent and Trademark Office for two US Patent Applications – composition of matter that includes ZS-9 and methods of treating hyperkalemia. The patents to be issued from these applications carry a patent term until at least 2032. In addition, the company will seek patent protection for manufacturing discoveries, including new in-process controls and starting materials. We believe additional allowances and patents will be issued in the coming year to help build out the IP around ZS-9.

In addition to IP, there are a number of non-IP protections that arise from the proprietary know-how and cost associated with producing ZS-9.

### **Pipeline**

Over time, ZS Pharma will aim to build a pipeline of products using its proprietary zirconium silicate technology, which provides the opportunity to target indications susceptible to treatment by non-absorbed binders in the GI tract. ZS Pharma is in nonclinical development of ZS-1 and plans to continue to evaluate zirconium silicate technology for other indications.

#### **ZS-1 – A Longer-Term Opportunity**

**ZS** Pharma is using its proprietary drug discovery technology to develop a non-absorbed nonclinical product candidate called **ZS-1**. ZS-1 is being designed to trap ammonium ions and is being evaluated for the treatment of disorders where elevated ammonium levels are believed to play a role, such as hepatic encephalopathy (HE) and urea cycle disorders (UCD).

It is estimated that there are approximately 8 million people in the US at risk for chronic disease. Of those, there are more than 750,000 cases of cirrhosis with up to 45% developing hepatic encephalopathy (HE). The prognosis for HE is poor with an estimated 58% mortality rate at one year and a 77% mortality rate at three years. Although exact incident rates are unknown, several sources estimate that UCDs occur in approximately 1 in 8,000 births worldwide.

**ZS** Pharma has developed a nonclinical and clinical plan, but has not yet initiated IND-enabling clinical studies for **ZS-1**. As substantially all resources will be initially focused on the advancement of ZS-9 through NDA submission and commercialization, we have not included ZS-1 in our forecast.

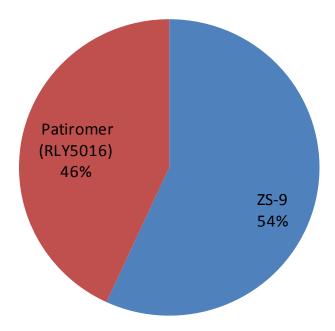
# **BMO Physician Feedback**

#### **Our Physician Surveys**

We conducted two physician surveys in June to get physician feedback on ZS-9 and hyperkalemia.

Based on a review of selected clinical data we provided the physicians concerning both drugs, approximately 54% of respondents we surveyed were more likely to use ZS-9 over Patiromer. Some of the common reasons for the preference of ZS-9 included better side effect data, tolerability, efficacy, quick onset, and its selective trapping.

Exhibit 16: Which product are you more likely to use?



#### **Follow-Up Comments:**

#### ZS Pharma's ZS-9

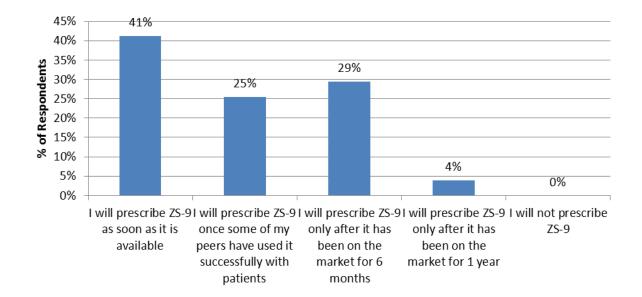
- Better side effect profile, more familiar with drug
- Effective with few side effects
- No side effects mentioned
- For acute cases
- Appears more feasible
- Dialysis used
- Well tolerated compared with placebo
- It looks like Relypsa gives more data about the reduction in K, but I do not see any mention of tolerance/safety
- Clinical results showing maintenance of normal potassium levels with RAAS blockade and safer side effects
- Not enough information about trials to say either is better
- I like the simplicity of an inorganic compound that will bind potassium without the need for polymers
- No GI side effects mentioned
- Has made it to phase 3 trials. New mechanism
- Appears safe and effective throughout the gut but did not comment on the adverse effects
- Good patient divvy
- Appears more promising, K control for extended periods and virtually free of side effects
- Highly selective for potassium
- Doesn't affect other electrolytes. Safe/well tolerated.
- Appears better tolerated
- Better GI side effect profile. Can be used for extended periods of time.
- Better tolerance and efficacy
- Seems more effective
- It is the more novel agent
- Fast
- Can use it for longer duration and clinical phase 3 trial
- Not listing GI side effects
- Easier to comply with
- Safety in phase 3 trials
- Seems more effective based on data

#### **Relypsa's Patiromer (RLY5016)**

- Seems safer
- Can be dosed less frequently. It comes as a powder that can be easily administered with food or water
- More effective clinical data
- Good safety, efficacy and extended control
- It's further along studies
- More advanced in trials
- Risk of severe GI side effects that can be fatal, including GI necrosis, bleeding and perforation
- Milder
- Reduction of 1 mEq/L and availability of long-term data
- More familiarity
- Tested in broad array of subjects
- Feel more comfortable to use it
- More is known about it
- As a cardiologist, I'm most likely to use this in heart failure patients. I appreciate that a specific study (albeit small) was dedicated to this patient population.
- HF, CKD, and ESRD patients
- Daily long-term use has appeal for chronic hyperkalemia
- Appears safe from above description
- Phase 3 data is already available
- Tolerability exceeds Kayexalate
- Can be used across many patient demographics.
   Minimal med interaction.

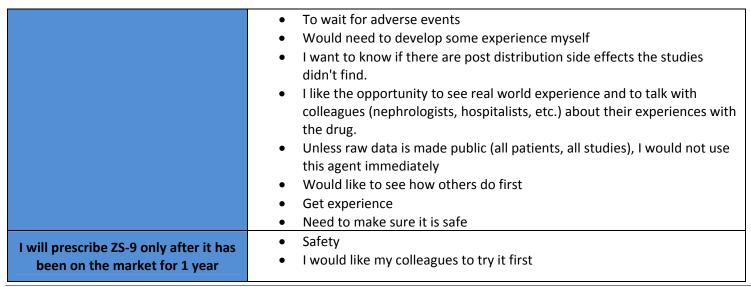
We believe that physicians will be quick to adopt ZS-9 in the treatment of hyperkalemia. Approximately 95% of respondents said they would adopt ZS-9 within six months of being on the market.

Exhibit 17: Which of the following best describes how you will adopt ZS-9 for the treatment of hyperkalemia?



# **Follow-Up Comments:**

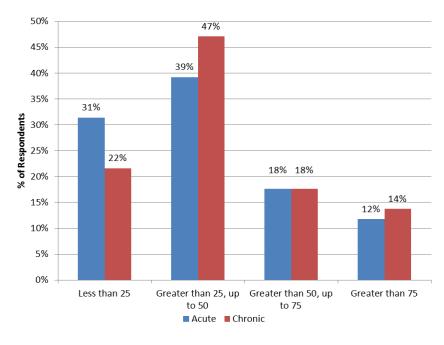
	Typically I am an early adopter of new therapies
	Will try when approved
	As an alternative to Kayexalate
	<ul> <li>It's very effective for acute hyperkalemia</li> </ul>
	<ul> <li>If safety similar to placebo feel comfortable starting use right away</li> </ul>
	<ul> <li>The need of better antikalemic measures and able to take advantage of</li> </ul>
	RAAS blockade in diabetics who are prone to this abnormality. Ease of
	administration and maintenance of potassium at normal levels for long
	time, so minimizing frequent lab testing and safer side effects
	<ul> <li>I need to give it a try with many of my more difficult to treat</li> </ul>
	hyperkalemic patients
	<ul> <li>Safe profile so reasonable to try</li> </ul>
I will prescribe ZS-9 as soon as it is	<ul> <li>I will already read the FDA review and viewed the studies. If needed and</li> </ul>
available	is safe, I would not wait. The only obstacle if the above are met, is the
	price.
	To see the effect
	<ul> <li>Need to see efficacy</li> </ul>
	Appears well tolerated
	To try its efficacy
	<ul> <li>Real breakthrough, needed notch</li> </ul>
	Efficacy supported by clinical data
	<ul> <li>I have many patients with chronic or recurrent hyperkalemia who would</li> </ul>
	benefit from an agent to control this problem
	<ul> <li>Because it's a very effective option and rapid onset of action</li> </ul>
	<ul> <li>Need to gain my own experience with it</li> </ul>
	Need new drug
	<ul> <li>Would prefer Patiromer over ZS-9; but having said that would use ZS-9</li> </ul>
	over SPS
	Kayexalate already works OK, want to see evidence of superiority of the
	new product
	Usually I am not the first one to use
I will prescribe ZS-9 once some of my	Do not typically jump on new products until there is more experience
peers have used it successfully with	I like to wait for others to use
patients	Would like to see effects in my patient populations before jumping on
	band wagon
	I am usually cautious
	I am typically an earlier adopter of new medications
	Would like to see some success first
	I am usually cautious  The state of the
	To get some experience with the drug
1 11 11 1 5 1	Avoid early complications pharmacy availability
I will prescribe ZS-9 only after it has	Wish to make sure the medication is safe and well tolerated
been on the market for six months	Experience
	I prefer to wait for additional safety data or concerns to emerge
	<ul> <li>I always wait for drugs six months prior to use</li> </ul>



Source: BMO Capital Markets Investor Survey (n=51), June 2014.

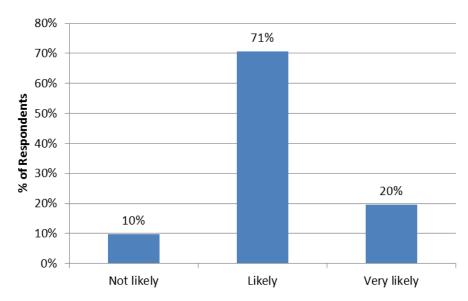
In addition, we believe physicians view ZS-9 as a treatment option for a large percentage of their current patients. When respondents were asked for what percentage of existing hyperkalemic patients they would prescribe ZS-9, 70% said they would prescribe ZS-9 in more than 25% of their acute patients and 80% said they would prescribe ZS-9 for more than 25% of their chronic patients. In addition, 30% of respondents said they would prescribe ZS-9 for more than 50% of their acute patients and 31% said they would prescribe ZS-9 for more than 50% of their chronic patients.

Exhibit 18: If approved, what percentage of your hyperkalemic patients do you anticipate you would prescribe ZS-9 to for each level of severity?



As many patients are not properly treated for CKD, HF, and diabetes due to the risk of developing hyperkalemia, we believe ZS-9 will radically alter these markets and allow for better patient treatment. In our survey, 91% of respondents said they were "likely" or "very likely" to start patients back on RAAS therapies once ZS-9 has brought potassium back down to normal levels.

Exhibit 19: For patients who were taken off of RAASi medications due to causing or worsening hyperkalemia, how likely are you to start patients back on RAASi therapies once ZS-9 has brought potassium levels back to normal range?

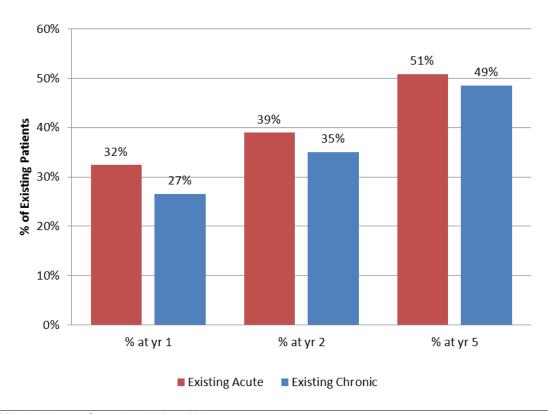


#### **Exhibit 20: Physician Concerns with Kayexalate**

# What concerns do you have with treating hyperkalemia with the polymer resin sodium polystyrene sulfonate (SPS)/Kayexalate?

- No concerns
- Concerns are: 1) Diarrhea which the patient does not always like 2) colonic necrosis when given as an enema 3) no clinical studies done approved by the FDA
- GI side effects
- No concerns
- Bowel necrosis, too much lowering of serum potassium, bad taste
- Hard to monitor
- Unpredictable and constipation
- Main issues are GI discomfort and uneven treatment response
- Not very efficient
- Ineffective risk of sorbitol-induced bowel necrosis constipation and diarrhea
- Allergies & CHF
- Compliance
- Bowel perforation
- Compliance in long term and GI issues with multiple use
- Availability at pharmacies, bowel necrosis, cost, tolerability
- Taste
- · Patients don't like consuming it and takes time to get the potassium down
- It takes a long time to bind and remove potassium
- The risk of colonic ischemia with rectal Kayexalate
- No concerns. Most times I can change dose of other medication causing hyperkalemia
- It is generally not well tolerated by patients powder form taken PO in water is very gritty; suspension in sorbitol causes diarrhea and is not very palatable or easy to store; I do not use the rectal suspension for enemas due to concern regarding colonic ischemia and perforation
- GI side effects
- No concerns because short-term option
- Bowel obstruction. Chronic use
- Colon obstruction
- Ischemic and necrotic bowel

Exhibit 21: What percentage of your EXISTING acute and chronic hyperkalemic patients do you think you would use ZS-9 on for each of the following time periods below?



## Management

Robert Alexander, Ph.D., Chief Executive Officer. Dr. Alexander has served as a member of the company's board of directors since October 2012 and has served as CEO since December 2013. Prior to 2013, Dr. Alexander served as director at Alta Partners, acted as executive chairman and interim CEO of SARcode Biosciences (acquired by Shire plc in April 2013), principal in MPM Capital's BioEquities fund, and joined Genentech (now a member of the Roche Group) after completing his post-doctoral fellowship at Stanford University in the Pathology department. He also holds a Ph.D. in Immunology from the University of North Carolina and a B.A. in Zoology from Miami University of Ohio.

**Alvaro Guillem, Ph.D., Co-Founder, President.** Dr. Guillem is a co-founder of ZS Pharma and has served as president and a member of the board of directors since 2008. He served as the CEO from February 2008 to December 2013 and is a veteran of the pharmaceutical industry with over 30 years of leadership experience in bringing new therapies to market at both well-established and start-up companies. Prior to ZS Pharma, Dr. Guillem held the role of VP of Quality and Scientific Affairs at Ash Access Technology, held senior positions at Genzyme/Bone Care, and worked at Adams Respiratory. Dr. Guillem holds a B.S. in chemistry from Mary Washington University and a Ph.D. in Chemistry from Virginia Commonwealth University.

**D.** Jeffrey Keyser, RPh, J.D., MPA, Ph.D., Co-Founder, Secretary and Chief Operating Officer. Dr. Keyser is a co-founder and has served as secretary, COO, and a member of the board of directors since 2008. Dr. Keyser has over 30 years of experience in the pharmaceutical industry. Prior to 2008, he served as the chief compliance officer and VP of Regulatory Affairs at Encysive, VP of Development and Regulatory Affairs at Adams Respiratory, and previously held senior management positions at Medeva Americas, Marion Merrell Dow, Marion Laboratories, and Abbott Laboratories. Dr. Keyser has experience in regulatory, medical, clinical, and product development and has directed efforts to develop, prepare and secure approvals of numerous INDs and NDAs. He received his B.S. in pharmacy and J.D. from Creighton University, holds an MPA from the University of Missouri at Kansas City and a Ph.D. in Economics from the University of Texas at Dallas.

**Todd A. Creech, MBA, Chief Financial Officer and Treasurer.** Mr. Creech has served as chief financial officer since August 2013 and as treasurer since February 2014. Prior to ZS Pharma, Mr. Creech was CFO and vice president of Business Development at SARcode Biosciences (acquired by Shire plc in April 2013), CFO of Sirion Therapeutics, worked with NovaQuest, and cofounded Centice in 2003. In addition, he has 10 years of biotech- and high-tech-specific consulting experience from his time at SRI International and Anderson Consulting. Mr. Creech holds undergraduate degrees in finance and accounting from Miami University of Ohio and an MBA from Duke University.

Henrik Sandvad Rasmussen, M.D., Ph.D., Chief Medical Officer, and Chief Scientific Officer. Dr. Rasmussen has served as CMO and CSO since October 2012. Before joining ZS Pharma, he served as president and CEO of Rasmussen Biotech and Pharma Consulting, held the positions of corporate VP and head of Clinical Development and Medical and Regulatory Affairs at Novo Nordisk, and served as chief medical officer for Nabi Biopharmaceuticals and for Genvec. In addition, he served as VP for Clinical Research and SVP for Clinical Research and Regulatory Affairs at British Biotech, and international clinical project manager and global study director for

cardiovascular drug development at Pfizer Central Research. Dr. Rasmussen has led numerous global development programs and regulatory filings worldwide, including NDAs. He has over 150 published peer-reviewed papers in therapeutic areas including nephrology, cardiology, and diabetes. Dr. Rasmussen received his M.D. and Ph.D. from the University of Copenhagen in Denmark and is trained in internal medicine and cardiology.

Cynthia Smith, MS, MBA, Chief Commercial Officer. Ms. Smith has served as chief commercial officer since June 2013. Prior to 2013, Ms. Smith was at Affymax, most recently in the position of VP of Market Access and Commercial Development, held various leadership positions at Merck, and served in the White House Office of Management and Budget during the Clinton Administration. Ms. Smith earned her BA. from the University of North Carolina at Chapel Hill, her MS in public policy from the Eagleton Institute at Rutgers University, and her MBA from the Wharton School at the University of Pennsylvania.

# **Valuation**

 We believe investors may look at a variety of methods of valuing ZS Pharma, including DCF, discounted earnings, multiple of sales, and peer comparisons. Our primary valuation method is DCF, and as a secondary measure, we consider an earnings multiple discounted to the present.

- We expect ZS-9 to be launched in 4Q16 with peak market share of 12% for total ZS-9 addressable US CKD patients and 12% of total ZS-9 addressable US HF patients in 2020. In addition, we believe ZS Pharma will be able to capture a share of the existing Kayexalate market with peak share of 35% in 2020.
- We assume ZS Pharma will market its own products in the US and will receive royalties from expected partnerships in Europe and Japan.
- We have risk adjusted our sales forecasts and are modeling a net price of \$543.75 per monthly prescription, with a duration of two months. Our revenue forecasts may reflect less than half of actual eventual use, leaving substantial room in our forecasts as clinical successes are met.
- Our forecasts do not include any additional development of ZS-1.
- We expect sales in 2018 of \$269 million, 2019 sales of \$392 million, and 2020 sales of \$482 million.
- We expect ZS Pharma to have net income of approximately \$86 million in 2018, \$149 millon in 2019, and \$155 million in 2020.

# **Exhibit 22: BMO EPS Estimates**

	2014	2015	2016	2017	2018	2019	2020
BMO EPS Estimates	(\$3.90)	(\$3.10)	(\$2.13)	\$0.84	\$3.38	\$5.82	\$6.07

Source: BMO Capital Markets

- We are taking very conservative approach on valuation, by delaying the timeline by six months and using a 15% discount rate in our DCF. We also use an 8x terminal multiple, which is about a 30% discount to where the specialty pharmaceutical industry is trading on average.
- Our DCF calculation leads to a valuation of \$786 million and a price target of \$38.
- For peers, we believe that Keryx Biopharmaceuticals, Ophthotech, Portola, Raptor, Relypsa, Hyperian, and AMAG may be the comps most investor compare ZS Pharma to

   all life sciences companies that are developing and/or marketing products focused on comparable market opportunities.
- The best comparable company is Relypsa, a specialty pharma company that went public in November 2013, at a post-money valuation of \$350 million and has a current market capitalization of \$795 million.

• On a discounted earnings basis, if one were to take our 2018 EPS estimate of \$3.38 and discount it back three years by 15% and apply a 15x multiple, the resulting target price would be \$34, and if one were to discount it 20% a year and apply a 20x multiple, the resulting price target would be \$39.

**Exhibit 23: ZS Pharma Discounted Cash Flow Statement (\$ millions)** 

WACC Terminal Value EV/EBITDA Multiple	15.0% 8.0x							
Unlevered Free Cash Flows		2014	<u> 2015</u>	<u>2016</u>	<u> 2017</u>	<u>2018</u>	2019	2020
		2014	<u>2013</u>	2010	2017	2010	2013	2020
Net Sales Growth Rate		\$0.0	\$0.0	\$17.4	\$136.4 683.2%	\$269.0 97.3%	\$392.4 <i>45</i> .9%	\$481.9 22.8%
EBIT <i>Margin</i>		(\$56.8)	(\$74.3)	(\$52.1)	\$25.7 18.9%	\$101.8 <i>37.8%</i>	\$175.2 <i>44.7%</i>	\$222.0 46.1%
Pre-tax income		(\$58.6)	(\$75.4)	(\$53.0)	\$25.2	\$101.7	\$175.2	\$222.0
Tax		\$0.0	\$0.0	\$0.0	(\$3.9)	(\$15.3)	(\$26.3)	(\$66.6)
Tax rate		0.0%	0.0%	0.0%	15.0%	15.0%	15.0%	30.0%
EBIAT		(\$56.8)	(\$74.3)	(\$52.1)	\$21.9	\$86.5	\$148.9	\$155.4
Plus: Depreciation and Amortization		\$1.4	\$1.5	\$1.6	\$1.7	\$1.8	\$1.8	\$1.9
Less: Capital Expenditures		(\$12.1)	(\$16.0)	(\$16.0)	(\$15.0)	(\$15.0)	(\$15.0)	(\$15.0)
Less: Change in Net Working Capital		\$0.7	\$2.1	(\$6.0)	\$3.2	(\$0.7)	\$3.0	\$2.3
Unlevered Free Cash Flow	=	(\$66.7)	(\$86.7)	(\$72.5)	\$11.7	\$72.6	\$138.8	\$144.7
Cumulative Unlevered FCF Terminal Value <sup>2</sup>	\$175.22 \$1,791.8	0.5	1.5	2.5	3.5	4.5	5.5	6.5
PV of Free Cash flow PV of Terminal Value	(\$24.0) \$722.4	-\$66.7	-\$86.7	-\$72.5	\$7.2	\$38.7	\$64.3	\$58.3
Implied Enterprise Value	\$698.3		/ Value Sensitivi	•				
Plus: Cash & Equivalents (4Q14)	\$102.4	F	EBITDA Multiple			1		
Less: Total Debt (1Q14)	\$15.0	иасс	\$37.96	7.0x	8.0x	9.0x		
Implied Value of Equity Diluted Shares Outstanding	\$785.8 20.7	Ä	14.0% 15.0%	\$35.78 \$33.60	\$40.40 <b>\$37.96</b>	\$45.02 \$42.32		
Implied Value per Share	\$37.96		16.0%	\$31.55	\$35.67	\$39.79		

Sources: Company reports and BMO Capital Markets estimates.

## **Risks**

• Manufacturing: ZS Pharma plans to manufacture all of its clinical and commercial drug supply of ZS-9, which could be costly and subject to regulatory or other delays. We visited the company's main manufacturing facility in Texas and have taken a slightly more conservative approach to the timeline for completion of construction, delaying the company's timeline by approximately six months. However, a construction delay would likely not affect the estimated filing timeframe of 1H15, but perhaps would affect the FDA's turnaround time on approving the facility.

- **Competition:** Relypsa is also developing a product for hyperkalemia that is slightly ahead of ZS-9 in the development process. We have spoken with Relypsa and believe its product, Patiromer, is a credible competitor. However, the addressable market is so large that we believe even if the company's take a 50/50 split in market share, ZS Pharma will see significant profits in the future.
- **Financing:** ZS Pharma will likely require additional financing to achieve its goals, and a failure to obtain this capital when needed could cause a delay or termination of the product development, operations, or commercialization efforts.
- Operating history: ZS Pharma has a limited operating history and has incurred significant losses since its inception, and we expect it will continue to incur losses for the foreseeable future.
- **Limited pipeline:** ZS Pharma is substantially dependent on the success of its only product candidate in clinical development, ZS-9. Even if ZS-9 receives approval, there is risk that it will fail to achieve a broad degree of physician and consumer acceptance for necessary commercial success.
- **IP protection:** Granted patents expire in 2019, but regulatory exclusivity and the 30-month stay would effectively stop competition until 2023-2024. Filed patents, if granted, will expire in 2032-2033. ZS Pharma has already received notice of allowance for additional patents that should extend the patent protection beyond 2030.

# **Summary**

We believe ZS Pharma offers a potential game-changing opportunity in the hyperkalemia treatment market.

We believe ZS-9, if approved, has the potential to greatly expand and rapidly alter the chronic kidney disease, diabetes, and chronic heart failure markets by addressing an unmet medical need to treat hyperkalemia. Current treatment options often lead to hyperkalemia, hindering a physician's ability to effectively treat these underlying diseases. If approved, we believe ZS-9 will be likely be readily adopted and split the hyperkalemic market with Relypsa's Patiromer if approved. We believe that Relypsa's further advancement in clinical studies is not a barrier for ZS Pharma to enter the market, but ZS Pharma will likely benefit from the increased attention on this unmet medical need. Based on the data so far and our physician feedback, we believe that ZS Pharma's drug will be preferred if both drugs are on the market and have similar marketing efforts.

Our valuation results in a \$38 price target, which is approximately 29% higher than where the shares are trading. We think longer term, ZS Pharma shares have a potential to be several times higher than where they are today if ZS-9 is approved, given our current forecasts are risk adjusted to be approximately one-fourth of what our physician feedback on intended use would be. That is, we have a market share assumption of 12% in 2020, while physician feedback is that they would use ZS-9 in approximately 50% of their patients with hyperkalemia. Our conservatism assumes two products on the market splitting the intended share and risk adjusting that share by 50%. We note that if we raise this to 25%, we estimate ZS shares would be worth approximately \$86.

However, with this potential reward investors must also be cognizant of the potential risks. At present, ZS Pharma is focused solely on the development of ZS-9 and if it is not approved, fails, or is delayed, ZS Pharma shares could significantly lose their value.

Given the rise in both Relypsa, the main competitor, and ZS Pharma's shares, we believe investors see potential for both companies to gain share in a large, underserved hyperkalemic market.

Overall, we believe ZS Pharma's ZS-9 represents a potential paradigm shift in the hyperkalemic market, and we are initiating with an Outperform rating.

Exhibit 24: ZS Pharma Income Statement (\$ millions, except per share data)

ZS Pharma Income Statement	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Net revenue for CKD patients					\$13.1	\$99.2	\$187.1	\$270.0	\$327.2
Net revenue for HF patients					\$2.9	\$27.2	\$41.3	\$60.1	\$72.9
ZS-9 episodic net revenues					\$1.4	\$8.4	\$27.8	\$33.4	\$39.0
ZS US net revenue					\$17.4	\$134.8	\$256.3	\$363.5	\$439.0
EU revenue (assumes ~50% of US price) Japan revenue (assumes ~20-30% of US price) Ex-US royalty rate					\$0.0 \$0.0	\$8.0 \$0.0 20%	\$60.7 \$3.2 20%	\$114.4 \$30.1 20%	\$165.0 \$49.3 20%
Ex-US royalty revenue					\$0.0	\$1.6	\$12.8	\$28.9	\$42.9
ZS Pharma Income Statement	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Total revenues % growth	\$0.0	\$0.0	\$0.0	\$0.0	\$17.4	\$136.4	<b>\$269.0</b> 97.3%	<b>\$392.4</b> 45.9%	\$481.9 22.8%
cogs	\$0.0	\$0.0	\$0.0	\$0.0	\$3.5	\$27.0	\$46.1	\$54.5	\$65.9
COGS as % of US sales					20.0%	20.0%	18.0%	15.0%	15.0%
Gross profit Gross margin	\$0.0	\$0.0	\$0.0	\$0.0	<b>\$13.9</b> 80.0%	<b>\$109.4</b> 80.2%	<b>\$222.9</b> 82.9%	<b>\$337.9</b> 86.1%	<b>\$416.1</b> 86.3%
R&D	\$7.0	\$24.5	\$43.6	\$36.0	\$20.0	\$20.2	\$25.6	\$36.3	\$41.7
R&D as % of US sales S&M	\$0.0	\$0.0	\$4.4	\$29.9	<i>114.9%</i> \$39.0	15.0% \$45.9	10.0% \$64.1	10.0% \$80.0	9.5% \$91.1
S&M as % of US sales G&A	\$1.1	\$7.7	\$8.9	\$8.4	224.0%	34.1% \$5.4	25.0% \$10.3	22.0%	20.8% \$17.6
G&A as % of US sales	Φ1.1	Φ1.1	\$0.9	<b>Ф</b> 0.4	\$1.3 7.4%	4.0%	4.0%	\$14.5 4.0%	4.0%
Royalties					\$5.8	\$12.2	\$21.2	\$31.8	\$43.6
Operating profit Operating margin	(\$8.1)	(\$32.2)	(\$56.8)	(\$74.3)	(\$52.1)	<b>\$25.7</b> 18.9%	<b>\$101.8</b> 37.8%	<b>\$175.2</b> <i>44.7%</i>	<b>\$222.0</b> 46.1%
Interest expense (income) Other expense (income)	\$2.1 \$0.1	(\$0.0) \$1.4	\$0.5 \$1.3	\$1.2 \$0.0	\$0.9 \$0.0	\$0.5 \$0.0	\$0.1 \$0.0	\$0.0 \$0.0	\$0.0 \$0.0
Pretax income	(\$10.3)	(\$33.6)	(\$58.6)	(\$75.4)	(\$53.0)	\$25.2	\$101.7	\$175.2	\$222.0
Pretax margin Taxes	\$0.0	\$0.0	\$0.0	\$0.0	\$0.0	18.5% \$3.8	37.8% \$15.3	44.7% \$26.3	46.1% \$66.6
Tax rate	0.0%	0.0%	0.0%	0.0%	0.0%	15.0%	15.0%	15.0%	30.0%
Net income Preferred stock accretion	(\$10.3)	(\$33.6)	(\$58.6) (\$0.2)	<b>(\$75.4)</b> \$0.0	<b>(\$53.0)</b> \$0.0	<b>\$21.4</b> \$0.0	<b>\$86.4</b> \$0.0	<b>\$148.9</b> \$0.0	<b>\$155.4</b> \$0.0
	(\$0.2)	(\$0.7)		•					·
Net income to common stockholders Net margin	(\$10.5)	(\$34.3)	(\$58.8)	(\$75.4)	(\$53.0)	<b>\$21.4</b> 15.7%	<b>\$86.4</b> 32.1%	<b>\$148.9</b> 38.0%	<b>\$155.4</b> 32.3%
Shares out (diluted)	1.6	1.6	15.1	24.3	24.9	25.6	25.6	25.6	25.6
Earnings per share EPS % growth	(\$6.74)	(\$21.84)	(\$3.90)	(\$3.10)	(\$2.13)	\$0.84	<b>\$3.38</b> 303.3%	<b>\$5.82</b> 72.3%	\$6.07 4.3%
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Source: Company Reports and BMO Capital Markets Estimates

Exhibit 25: ZS Pharma Balance Sheet (\$ millions)

ZS Pharma Balance Sheet	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Assets									
Cash and cash equivalents	\$24	\$9	\$102	\$128	\$78	\$88	\$160	\$303	\$452
Restricted cash	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Accounts receivables, net	\$0	\$0	\$0	\$0	\$3	\$20	\$48	\$75	\$101
Inventories	\$0	\$0	\$0	\$7	\$1	\$7	\$13	\$20	\$24
Prepaid expenses and other	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Total current assets	\$24	\$9	\$103	\$135	\$82	\$116	\$223	\$397	\$577
PP&E, net	\$1	\$5	\$16	\$30	\$45	\$58	\$71	\$84	\$97
Other non-current assets	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Total assets	\$26	\$14	\$118	\$165	\$127	\$174	\$294	\$482	\$675
Liabilities									
Current liabilities									
Accounts payable	\$1	\$1	\$2	\$9	\$2	\$12	\$22	\$27	\$31
Clinical accounts payable	\$0	\$0	\$1	\$1	\$1	\$1	\$1	\$1	\$1
Note payable - Insurance	\$0	\$0	\$2	\$0	\$0	\$0	\$0	\$0	\$0
Interest Payable	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Accrued liabilities	\$1	\$3	\$2	\$5	\$3	\$15	\$28	\$43	\$55
Current portion of capital lease		· 1			· 1				
obligation	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Other current liabilities	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Total current liabilities	\$2	\$5	\$7	\$15	\$6	\$28	\$51	\$72	\$88
Deffered rent	\$0	\$0	\$0	\$0	\$0	\$4	\$16	\$30	\$47
Lease incentive	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Note payable	\$0	\$0	\$15	\$14	\$9	\$4	\$0	\$0	\$0
Warrant liability - Common	\$0	\$0	\$2	\$0	\$0	\$0	\$0	\$0	\$0
Warrant liability	\$0	\$0	\$5	\$0	\$0	\$0	\$0	\$0	\$0
Series B redeemable preferred stock			**	'	'	,,,	'	'	
warrant liability	\$1	\$3	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Other			Ų ū	\$4	\$7	\$11	\$15	\$19	\$23
Total liabilities	\$3	\$8	\$29	\$33	\$22	\$48	\$81	\$120	\$158
Shareholder's Equity									
Series B convertible preferred stock	\$8	\$8	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Series C convertible preferred stock	\$27	\$43	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0
Series D convertible preferred stock	\$27 \$1	\$1	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0
Series A convertible preferred stock	\$0	\$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0
Common stock	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0	\$0 \$0
Additional paid-in capital	\$0 \$2	\$0 \$4	\$195	\$315	\$340	\$340	\$340	\$340	\$340
Defecit accumulated during the	پ پ	Ψ4	φ195	φυισ	φ3 <del>4</del> 0	φ3 <del>4</del> 0	φ340	φ3 <del>4</del> 0	φ3 <del>4</del> 0
development stage	(\$17)	(\$50)	(\$107)	(\$183)	(\$236)	(\$214)	(\$128)	\$21	\$176
Total equity	\$23	(\$50) \$6	(\$107) \$89	\$133	\$104	\$126	\$212	\$361	\$176 <b>\$517</b>
i otai equity	<b>Ψ</b> 23	φo	<b>\$09</b>	\$133	<b>Φ104</b>	\$120	<b>⊅∠1</b> ∠	\$301	φ <b>5</b> 17
Total liabilities and equity	\$26	\$14	\$118	\$165	\$127	\$174	\$294	\$482	\$675

Source: Company Reports and BMO Capital Markets Estimates

Exhibit 26: ZS Pharma Cash Flow Statement (\$ millions)

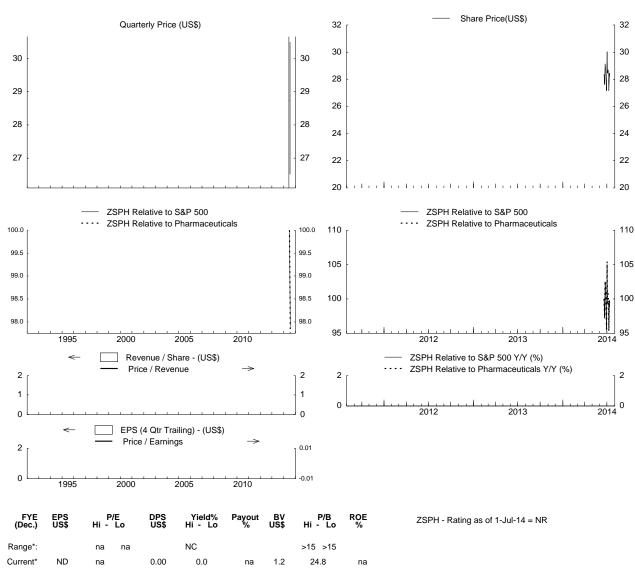
ZS Pharma Cash Flow	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Net earnings	(\$10)	(\$34)	(\$59)	(\$75)	(\$53)	\$21	\$86	\$149	\$155
Cash flows from operating activities:									
Depreciation and amortization	\$0	\$1	64	\$2	\$2	\$2	\$2	\$2	\$2
Amortization of lease incentive	\$0 \$0		\$1 (\$0)		\$2 \$0	\$2 \$0	\$2 \$0	\$2 \$0	\$2 \$0
		(\$0)	(\$0)	\$0					
Share-based expenses	\$0	\$2	\$3	\$4	\$4	\$4	\$4	\$4	\$4
Warrant expense	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Series B warrant mark-to-market expense	\$0	\$1	\$1	\$0	\$0	\$0	\$0	\$0	\$0
Amortization of deferred debt issuance costs	00	00	00						00
and discount	\$2	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Interest expense repaid in Series B preferred									
stock	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Loss on disposal of assets and other noncash									
income	\$0	(\$0)	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Changes in operating activities									
Accounts receivable	\$0	\$0	\$0	\$0	(\$3)	(\$18)	(\$28)	(\$26)	(\$27)
Inventories	\$0	\$0	\$0	(\$7)	\$6	(\$5)	(\$7)	(\$6)	(\$4)
Prepaid expenses and other	(\$0)	(\$0)	(\$0)	\$0	\$0	(\$0)	(\$0)	\$0	\$0
Accounts payable	\$0	\$1	\$0	\$7	(\$7)	\$10	\$9	\$6	\$4
Clinical accounts payable	\$0	\$0	\$1	\$0	\$0	\$0	\$0	\$0	\$0
Acrrued liabilities	\$0	\$2	(\$0)	\$2	(\$2)	\$12	\$13	\$15	\$12
Other current liabilities	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Deferred rent	\$0	\$0	\$0	(\$0)	\$0	\$4	\$12	\$14	\$17
Net cash provided by op activities	(\$7)	(\$27)	(\$52)	(\$68)	(\$54)	\$30	\$91	\$158	\$164
Cash flows from investing activities:									
Capital expenditures	(\$1)	(\$4)	(\$12)	(\$16)	(\$16)	(\$15)	(\$15)	(\$15)	(\$15)
Net cash provided by financing activities	(\$1)	(\$4)	(\$12)	(\$16)	(\$16)	(\$15)	(\$15)	(\$15)	(\$15)
Net cash provided by infahenig activities	(\$1)	(44)	(Ψ12)	(\$10)	(\$10)	(\$13)	(\$13)	(\$13)	(\$13)
Cash flows from financing activities:									
Proceeds (repayment) of note payable, net	\$1	\$0	\$15	(\$1)	(\$5)	(\$5)	(\$4)	\$0	\$0
Proceeds from issuance of stock options	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Proceeds from exercise of warrants	\$0	\$0	\$3	(\$9)	\$0	\$0	\$0	\$0	\$0
Proceeds from issuance of restricted stock	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Proceeds from Series A preferred stock, net	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Proceeds from Series B preferred stock, net	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Proceeds from Series C preferred stock, net	\$28	\$15	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Proceeds from Series D preferred stock, net	(\$0)	\$15	\$25	\$0	\$0	\$0	\$0	\$0	\$0
Principal payments on capital lease	\$0	(\$0)	(\$0)	\$0	\$0	\$0	\$0	\$0	\$0
Restricted cash	\$0	(\$0)	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Other items, net	\$0	\$0	\$2	\$0	\$0	\$0	\$0	\$0	\$0
IPO proceeds	\$0	\$0	\$112	\$120	\$25	\$0	\$0	\$0	\$0
Net cash provided by financing activities	\$29	\$30	\$157	\$110	\$20	(\$5)	(\$4)	\$0	\$0
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Source: Company Reports and BMO Capital Markets Estimates

Other companies mentioned (priced as of the close on July 11, 2014)

Relypsa (RLYP, \$23.50, Not rated)





Last Price ( July 10, 2014): \$28.21 Sources: IHS Global Insight, Thomson Reuters, BMO Capital Markets.

<sup>\*</sup> Current EPS is the 4 Quarter Trailing to Q1/2014.
\* Valuation metrics are based on high and low for the fiscal year.
\* Range indicates the valuation range for the period presented above.

#### IMPORTANT DISCLOSURES

#### **Analyst's Certification**

I, David Maris, hereby certify that the views expressed in this report accurately reflect my personal views about the subject securities or issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the specific recommendations or views expressed in this report.

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#### Company Specific Disclosures

1 - BMO Capital Markets has undertaken an underwriting liability with respect to this issuer within the past 12 months.

9 - BMO Capital Markets makes a market in this security.

# Methodology and Risks to Price Target/Valuation

Methodology: We arrive at our target price using a discounted cash flow analysis, a sector multiple applied to discounted earnings, and as a multiple of sales.

Risks: In addition to the normal risks inherent in pharmaceutical companies, such as regulatory, reimbursement, and competitive risks, our valuation of ZSPH carries several other risks. Among the risks to our valuation is ZSPH's dependence on approval of their lead product and anticipated sales and profitability to drive the value of ZSPH. Unseen side effects, safety issues, and competitive threats have not been taken into account in our valuation and if any of these were to emerge, it is likely ZSPH shares would be significantly and negatively impacted. ZSPH is currently running at a substantial loss, and with this fact comes several other risks, including the potential need for financing. One cannot be certain that ZSPH would be able to secure additional financing and at what cost. Our valuation does not include any value for ZSPH's additional product in the pipeline.

Distribution of Ratings (June 30, 2014)

Rating		BMOCM US	BMOCM US	BMOCM US	BMOCM	BMOCM	Starmine
Category	BMO Rating	Universe*	IB Clients**	IB Clients***	Universe****	IB Clients****	Universe
Buy	Outperform	44.1%	21.1%	67.5%	43.3%	58.6%	55.4%
Hold	Market Perform	50.9%	8.4%	31.3%	51.2%	39.9%	39.5%
Sell	Underperform	5.0%	3.4%	1.3%	5.5%	1.5%	5.1%

- \* Reflects rating distribution of all companies covered by BMO Capital Markets Corp. equity research analysts.
- \*\* Reflects rating distribution of all companies from which BMO Capital Markets Corp. has received compensation for Investment Banking services as percentage within ratings category.
- \*\*\* Reflects rating distribution of all companies from which BMO Capital Markets Corp. has received compensation for Investment Banking services as percentage of Investment Banking clients.
- \*\*\*\* Reflects rating distribution of all companies covered by BMO Capital Markets equity research analysts.
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#### Rating and Sector Key (as of April 5, 2013):

We use the following ratings system definitions:

OP = Outperform - Forecast to outperform the analyst's coverage universe on a total return basis

Mkt = Market Perform - Forecast to perform roughly in line with the analyst's coverage universe on a total return basis

Und = Underperform - Forecast to underperform the analyst's coverage universe on a total return basis on a total return basis

(S) = speculative investment;

NR = No rating at this time;

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