William Blair

ZS Pharma, Inc.

September 24, 2014

Positive Top-Line Readout of Second Phase III Trial (HARMONIZE), Full Data at AHA Late Breaker on November 17

- **After the close on Tuesday, September 23, ZS Pharma announced positive top-line results from HARMONIZE, its second Phase III study of ZS-9 in patients with hyperkalemia.** Top-line results of the study show that all three doses of ZS-9 tested (5 g, 10 g, and 15 g, once-daily) significantly reduced mean serum potassium below placebo over a 28-day treatment period. It was reported that the safety, tolerability, and adverse event profile was consistent with previous ZS-9 studies. We believe the company was limited in the amount of disclosure ahead of the complete data set for HARMONIZE to be presented and discussed at the 2014 Annual Meeting of the American Heart Association in a late-breaking platform session on November 17 in Chicago.

- **For HARMONIZE, 258 patients with hyperkalemia were enrolled in the study at 42 sites, including patients with congestive heart failure (CHF), chronic kidney disease (CKD), and diabetes, including those on a variety of renin-angiotensin-aldosterone (RAAS) inhibitor therapies.** As shown in exhibit 1, on page 2, after a 48-hour induction phase of 10 g of ZS-9 three times per day (similar to the company's previous onset-of-action study), patients were randomized into a maintenance phase of placebo, 5 g ZS-9, 10 g ZS-9, and 15 g ZS-9 once a day for 28 days. The primary endpoint of the study was the comparison of mean serum potassium levels from day 8 through day 28, with secondary endpoints being the proportion of normokalemic patients after the induction phase and during the 28-day maintenance period. In addition, patients can be continued into an open-label extension period (ZS004E) at the 10 g dose once a day, with 5 g dose titrations if necessary to maintain normokalemia. The closest trial from competitor Relypsa's (RLYP $21.00) was its Phase III Part B that assessed randomized withdrawal over the course of 28 days.

- **The company is on track to submit its NDA and MAA filings for ZS-9 in the first half of 2015. To date, the company has completed treatment of nearly 1000 patients, some of which have been on therapy for over five months**. As shown in exhibit 2, on page 3, the clinical trial program of ZS-9 has now completed three studies, a Phase II in 90 patients, the first pivotal Phase III trial in 753 patients, and the second pivotal Phase III trial (HARMONIZE) announced on Tuesday. The total anticipated size of the safety and efficacy database at regulatory filing will be large, with almost 1000 patients treated to date. In comparison, Relypsa will have tested its therapy for hyperkalemia, patiromer, in about 700 patients by its regulatory filing, which is guided to be completed in the fourth quarter of 2014, including a Phase I onset of action study in 25 patients, a Phase III Part A and Part B study in 301 patients, and a 52-week Phase IIb study in 306 patients. We believe ZS-9 has the best profile to date, one which we believe will be strengthened when the company reports longer-term safety data in 2015. But based on recent discussions with a leading hyperkalemia key opinion leader, Dr. Bertram Pitt, we note that the market for hyperkalemia therapies is large in the chronic setting, which may leave room for more than one successful therapy in the market.

ZS Pharma is a specialty pharmaceutical company located in San Mateo, California, focused on developing therapies based on highly selective ion trap chemistry.

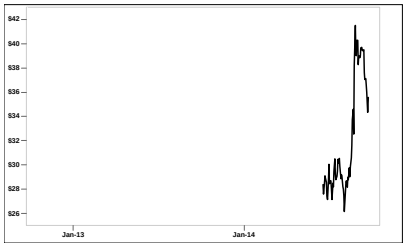
Stock Rating:	**Outperform**
Company Profile:	**Aggressive Growth**
Price Target:	$75.00
Symbol:	ZSPH (NASDAQ)
Price:	$38.05 (52-Wk.: $26-$43)
Market Value (mil.):	$792
Fiscal Year End:	December
Long-Term EPS Growth Rate:	
Dividend/Yield:	None

	2013A	2014E	2015E
Estimates			
EPS FY	$-8.52	$-3.18	$-2.94
CY		$-3.18	$-2.94
Valuation			
FY P/E	NM	NM	NM
CY P/E		NM	NM

Trading Data (FactSet)	
Shares Outstanding (mil.)	3
Float (mil.)	9
Average Daily Volume	168,753

Financial Data (FactSet)	
Long-Term Debt/Total Capital (MRQ)	0.0
Book Value Per Share (MRQ)	6.2
Return on Equity (TTM)	-235.2

Two-Year Price Performance Chart



Sources: FactSet, William Blair & Company estimates

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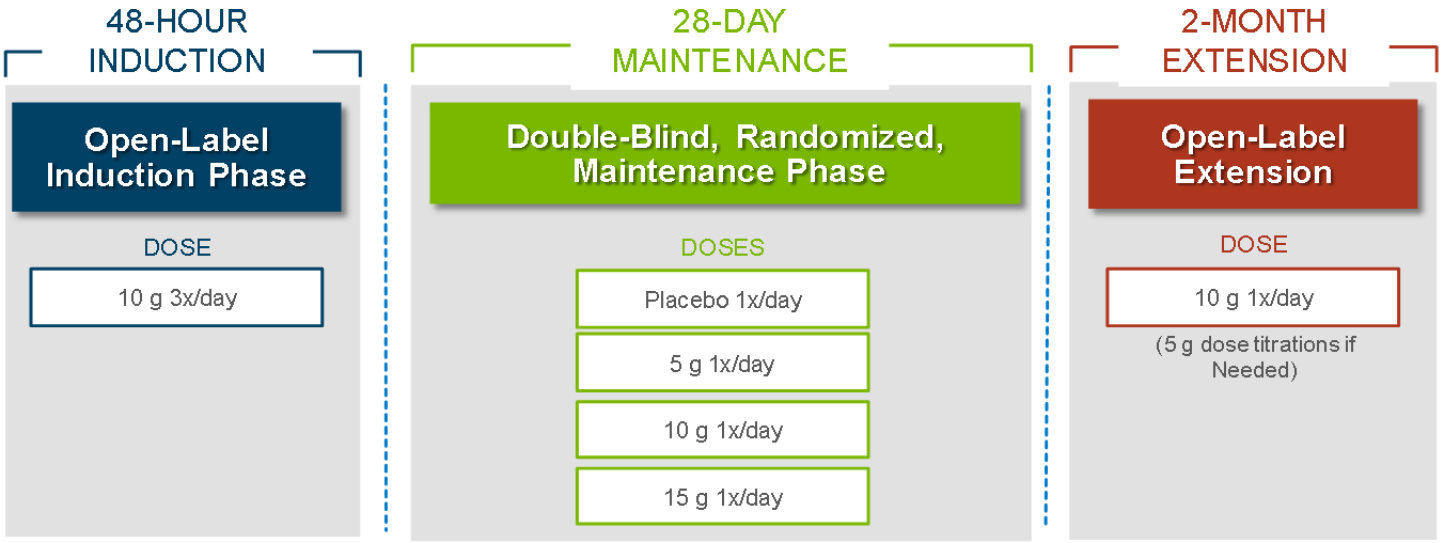
- **The questions remaining for Relypsa concern the onset of action and for ZS Pharma revolve around long-term efficacy.** The positive top-line readout reported on Tuesday shows that ZS-9 is effective, safe, and tolerable up to 28 days, double the length of the previous pivotal Phase III trial (14 days). However, we believe presentation of long-term safety data will be key to the success for ZS-9 in the chronic setting. Based on discussions with management, we believe the roughly 500-person open-label trial safety and efficacy study is progressing well; however, full data from the study will not be available until 2015. We believe data from the 52-week open label long-term study (ZS005) and the extension portion of HARMONIZE (ZS004E) are highly anticipated, and should solidify the ability of ZS-9 use to maintain normokalemia in the long term. To date, the safety profile of ZS-9 has been shown to be a major clinically differentiating factor from patiromer and Tuesday's press release stated that the safety results are consistent with previous studies (exhibit 4, page 3), making us continue to believe that ZS-9 is a best-in-class product. Our recent discussions with thought leaders also suggest that the primary site of action between the two products (patiromer is active in the colon, whereas ZS-9's site of binding is in the intestine) could favor ZS-9 in the acute setting, where most hyperkalemic patients are now diagnosed. We believe this is a major differentiator; if ZS-9 were to show rapid lowering of potassium levels, it may prove to be the best therapy in the acute setting, and following long-term data, which should be available in 2015, the product may be found ideal for rolling patients onto a maintenance therapy following an acute attack.

- **We continue to rate shares of ZS Pharma Outperform with a price target of $75 given our belief that ZS-9 holds a best-in-class profile for the treatment of the large hyperkalemia and maintenance of normokalemia market.** In total, we believe the hyperkalemia market exceeds 3 million patients in the United States alone with few good treatment options.

Exhibit 1
ZS Pharma, Inc.
HARMONIZE Study Design



Primary Endpoint: Comparison of mean serum K^+ levels from day 8 to day 28

Secondary Endpoints: Proportion of patients normokalemic after induction phase
Proportion of patients normokalemic during 28-day maintenance period

Source: Company reports

Exhibit 2
ZS Pharma, Inc.
ZS-9 and Patiromer Phase II and III Clinical Trial Programs

Patiromer			
Completed/Timeline	**Patient Types**	**N**	**Trial**
Completed	HK, CKD, Type II Diabetes, Hypertension	306	Phase IIb: 52-week safety & efficacy
Completed	HK with CKD	301	Phase III pivotal Part A/B
Completed	HK with CKD	25	Phase I onset-of-action
Total Anticipated Size of Safety Database at NDA Submission = Approx. 730 Total Patients			
ZS-9			
Completed/Timeline	**Patient Types**	**N**	**Trial**
Completed	Hyperkalemia, CKD	90	Phase II
Completed	Hyperkalemia regardless of etiology	753	Phase III pivotal
Completed	Hyperkalemia regardless of etiology	258	Phase III pivotal
2015	Hyperkalemia	750	Open-label long term
Total Anticipated Size of Safety Database at NDA Submission = Approx. 1,073 Total Patients			

Source: Relypsa and ZS Pharma Company Reports

Exhibit 3
ZS Pharma, Inc.
Change in Serum Potassium After Treatment With ZS-9 and Patiromer

Time Point	Patiromer	Dose	RLYP Study	ZS-9	Dose	ZSPH Study
48 hours	5.83 mEq/L -> 5.1 mEq/L	8.4g b.i.d.	Phase I Onset-of-Action	5.3 mEq/L -> 5 mEq/L	1.25g t.i.d.	ZS-003
				5.3 mEq/L -> 4.84 mEq/L	2.5g t.i.d.	Induction Phase
				5.3 mEq/L -> 4.76 mEq/L	5g t.i.d.	
				5.3 mEq/L -> 4.57 mEq/L	10g t.i.d.	
2 weeks	Mild HK: ~5.2 mEq/L -> ~4.8 mEq/L Moderate/Severe HK ~5.6 mEq/L -> 4.8 mEq/L	10g t.i.d	RLY5016-205 (AMETHYST-DN)	5.3 mEq/L ->4.71 mEq/L	5g q.d.	ZS-003
				5.3 mEq/L -> 4.55 mEq/L	10g q.i.d.	Maint. Phase
4 weeks	Mild HK: ~5.1 mEq/L -> ~4.65 mEq/L Moderate/Severe HK: ~5.8 mEq/L -> 4.5 mEq/L	Mild: 8.4 q.d. Mod/Sev HK: 8.4g b.i.d.	Phase III	Positive top-line		HARMONIZE
52 weeks	Mild HK: ~5.2 mEq/L -> ~4.6 mEq/L Moderate/Severe HK: ~5.65 mEq/L -> ~4.6 mEq/L	10-40g q.d.	RLY5016-205 (AMETHYST-DN)	Study Initiated in Q2 2014		ZS-005

Sources: ZS Pharma and Relypsa company reports

Exhibit 4
ZS Pharma, Inc.
Safety Measures From ZS-9 and Patiromer (RLY5016)

	Induction Phase (48 h)		Maintenance Phase (2 weeks)	
Safety Measurement	**Placebo**	**ZS-9**	**Placebo**	**ZS-9**
All Adverse Events	10.8%	12.9%	24.5%	25.1%
GI Events	5.2%	3.5%	3.7%	5.5%

Safety Measurement	**Placebo**	**RLY5016**
All Adverse Events	31%	54%
GI Events	6%	21%

Sources: Pitt et al. Eur Heart J 2011, Company Reports, William Blair & Company, L.L.C.

Valuation

We rate shares of ZS Pharma Outperform with a $75 price target. Our price target is derived from our net-present-value model for ZS-9 and applying a 75% probability of success (exhibit 5). Swing factors in our peak-year estimates include patient duration, which we estimate will reach six months; however, if ZS Pharma is successful in penetrating the chronic therapy market, this duration might hold upside. Currently, we anticipate peak sales for ZS-9 of $1.17 billion by penetrating 10% to 13% of the available patient populations within select markets.

Exhibit 5
Sum of the Parts Valuation

	Peak Sales	Discount Rate	Probability of Success	Peak Sales	Value Per Share
ZS-9	$1,170	11%	75%	2021	$ 72.40
Cash Per Share					$ 4.71
NPV of Future Losses Per Share					$ (2.38)
NPV Value					$ 1,808,567
NPV Value Per Share					$ 74.73

Source: William Blair & Company L.L.C. estimates

For per share numbers we use fully diluted share count of 24.2 million

Risks

Risks to an investment in ZS Pharma include the normal clinical, regulatory, and commercial risks in development-stage therapeutics companies.

IMPORTANT DISCLOSURES

William Blair was a manager or co-manager of a public offering of equity securities for ZS Pharma, Inc. within the prior 12 months.

William Blair is a market maker in the security of ZS Pharma, Inc. and may have a long or short position.

William Blair intends to seek investment banking compensation in the next three months from ZS Pharma, Inc.

Within the past 12 months William Blair has provided or is providing investment banking services to or has an investment services relationship with ZS Pharma, Inc.

Additional information is available upon request.

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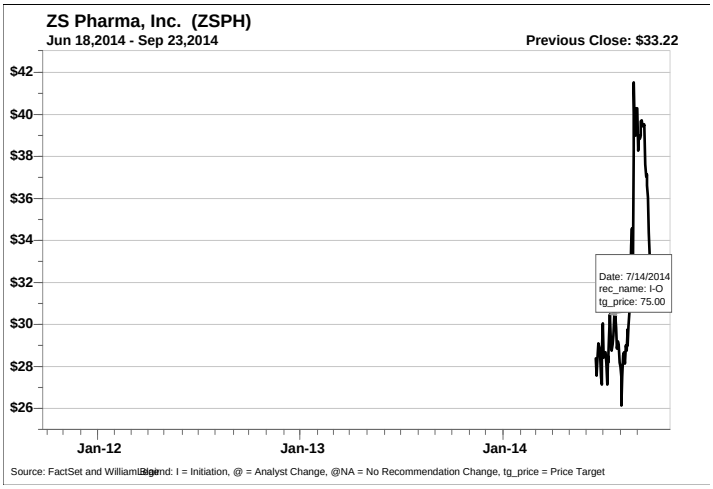
DOW JONES: 17,055.87
S&P 500: 1,982.77
NASDAQ: 4,508.69



Current Rating Distribution (as of 08/31/14)

Coverage Universe	Percent	Inv. Banking Relationships*	Percent
Outperform (Buy)	66	Outperform (Buy)	16
Market Perform (Hold)	31	Market Perform (Hold)	3
Underperform (Sell)	1	Underperform (Sell)	0

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