William Blair

ZS Pharma, Inc.

September 16, 2014

ZS-003 Heart Failure Subgroup Consistent With Overall Results, HARMONIZE Results Approaching, Maintain Outperform

- After the close on Monday, September 15, ZS Pharma announced results of a subgroup analysis of its previously announced Phase III clinical trial, ZS-003. The data was presented as part of a late-breaking clinical trial oral session at the Heart Failure Society of America's Annual Meeting in Las Vegas earlier in the afternoon. In the subgroup analysis, 147 normokalemic heart failure patients on RAAS (renin-angiotensin-aldosterone system) inhibitor therapy who received either 5 g or 10 g of ZS-9 once per day maintained serum potassium levels in the normokalemic range (between 3.5 mEq/L and 5 mEq/L) throughout the 12-day maintenance period with mean serum potassium of 4.7 and 4.5 mEq/L, respectively. These levels were significantly lower from the placebo group for both the 5 g dose ($p<0.009$) and 10 g dose ($p<0.002$), where the mean serum potassium levels increased above 5 mEq/L (hyperkalemic range). Results continue to suggest ZS-9 is effective in the treatment of hyperkalemia and maintenance of normokalemia during the 12-day maintenance period, a trend we do not anticipate changing during longer periods of treatment given the clean safety profile of ZS-9 and excellent tolerability to date. Outside of the continued efficacy of ZS-9, there continues to be no significant increase in adverse events in all dose levels and subgroups in the 753 patient ZS-003 study (1.25 g, 2.5 g, 5 g, and 10 g) when compared with placebo.

- **Latest subgroup analysis consistent with previous ZS-003 late-breaking oral/poster presentations.** Results from the subgroup of patients with heart failure are consistent with prior subgroup analyses that have been presented at other major cardiovascular and diabetes conferences throughout the year. These include subgroup analyses in patients with diabetes presented as a late-breaker at the American Diabetes Association Scientific Sessions in June, a subgroup analysis presented at a late-breaking poster presentation at the European Renal Association-European Dialysis and Transplant Association Congress in May, a late-breaking oral presentation at the American Society of Hypertension Annual Scientific Meeting in May, and a presentation at the National Kidney Foundation's 2014 Spring Clinical Meetings. As previously discussed by management, ZS-9 in all subgroups continues to show consistent efficacy and safety across the relatively heterogeneous patient population enrolled in ZS-003.

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

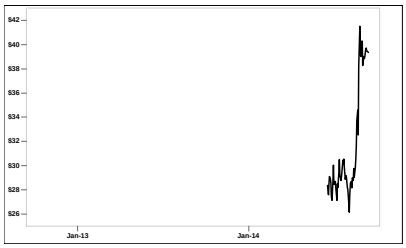
Symbol:	ZSPH (NASDAQ)
Price:	$37.63 (52-Wk.: $26-$43)
Market Value (mil.):	$783
Fiscal Year End:	December
Long-Term EPS Growth Rate:	
Dividend/Yield:	None

		2013A	2014E	2015E
Estimates				
EPS	Q1	NA	$0.02	NA
	Q2	NA	$-4.72	NA
	Q3	NA	$-0.74	NA
	Q4	NA	$-0.81	NA
	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	165,883

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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- **Given consistent ZS-003 results, we expect positive results from second Phase III study, HARMONIZE, expected in late September/October.** In the second quarter, ZS Pharma announced that it had completed enrollment of HARMONIZE (HyperkAlemia RandoMized interventiON multI-dose ZS-9 maintEnance clinical trial), the company's second Phase III study of ZS-9 for the indication of hyperkalemia (exhibit 1, on page 3). The study enrolled 258 patients with hyperkalemia 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 system (RAAS) inhibitor therapies. The company expects top-line data from the trial to read out as early as the next several weeks, with full data to be presented at an upcoming medical conference. In addition, ZS Pharma is rolling HARMONIZE patients into an extension study, which is expected to eventually provide one year of open-label safety, tolerability, and efficacy data; however, we are unsure if one year or only six months of data will be included in the initial label for ZS-9. During the second quarter, the company also began enrolling ZS-005, a 52-week open label safety and efficacy trial that should read out in 2015 and also supplement the company's regulatory filing (exhibit 2, on page 4). The company remains on track to file an NDA in the first half of 2015 and we continue to have a high conviction in the potential for success of ZS-9 in the long-term treatment of hyperkalemia and maintenance of normokalemia. We believe the product profile of ZS-9 continues to suggest a best-in-class product with a lower adverse effect profile than products currently on the market or under development given data to date and the underlying specificity ZS-9 holds in binding potassium.

- Regarding competitive programs, hyperkalemia development competitor Relypsa (RLYP $25.70), also announced data at Monday's late-breaking session. Although we were unable to attend the session, data in the company's press release continues to suggest ZS-9 may hold an improved potency for reducing potassium levels across a heterogeneous patient population. In the two-part Phase III trial conducted by Relypsa, the company noted a 1.06 mEq/L ($p<0.001$) reduction in potassium levels in patients with heart failure (HF), which was described as similar to those without HF during the non-placebo controlled Part A of the study. During the placebo-controlled portion of the study, Part B, the difference between placebo (22 HF, 30 non-HF) and patiromer (27 HF, 28 non-HF) was 0.64 mEq/L ($p<0.001$). The company stated that 8% of patients in the heart failure subgroup experienced recurrent hyperkalemia compared with 52% in the placebo group ($p<0.001$) and noted a similar trend in non-heart-failure patients (23% compared with 66%, $p<0.001$), with the absolute difference ranging from 43% to 44% between active and placebo. Given the size of the ZS-003 study (N=753), we believe the company's subgroup analysis is more robust with 147 normokalemic heart failure patients, three times more patients than the 49 patients included in the patiromer subgroup analysis. We will not receive data from ZS-9 long-term use until 2015, when the extension portion of ZS-004 and the long-term safety study ZS-005 report, although normokalemic levels on average are achieved throughout the 12-day treatment period of ZS-003 for the 5 g and 10 g doses, while placebo patients increased to above 5 mEq/L.

- The patiromer NDA submission is still on track for early in the fourth quarter, which we believe is approximately one to two quarters ahead of the NDA submission of ZS-9, which should occur in the first half of 2015. As shown in exhibit 3, on page 4, the market capitalizations of both ZS Pharma and Relypsa have been in the $750 million to $860 million range since August 25. And while investor interest now seems focused on handicapping the outcome of ZS-004 (HARMONIZE) and the resulting stock movement, we note that in the past Relypsa has reached a market cap of over $1.4 billion, suggesting significant upside is still possible if ZS-9 continues to look like a best-in-class agent.

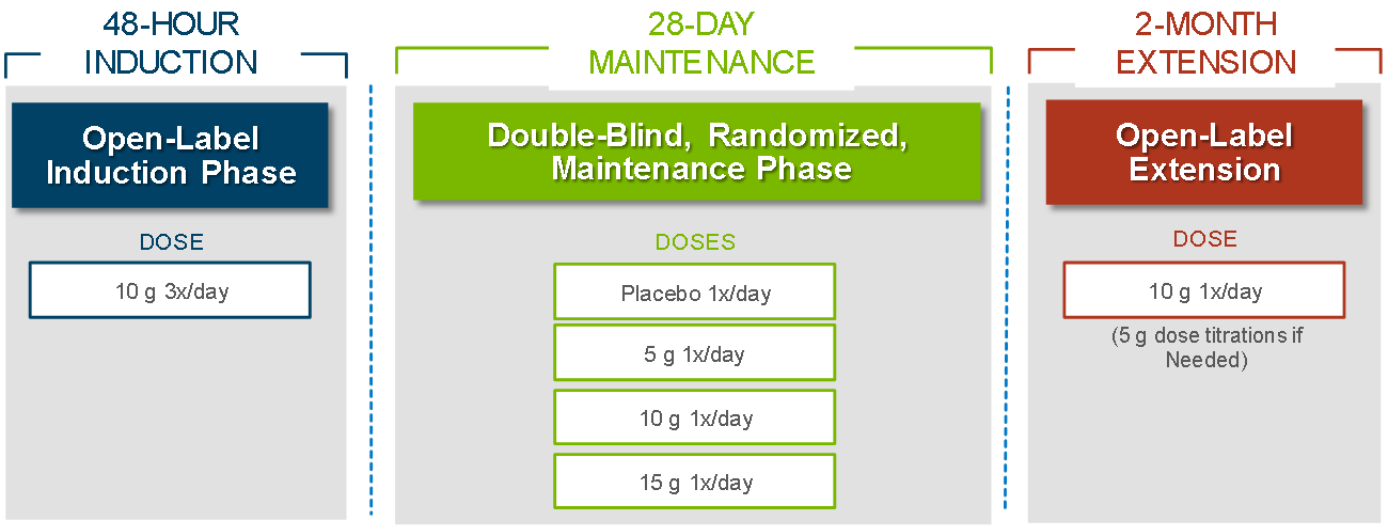
- As shown in exhibit 4, on page 4, the relative adverse event profile for patiromer seems to show a greater percentage of adverse events, and particularly GI events, in comparison with ZS-9. We believe these data show that ZS-9 has a best-in-class safety profile which is in line with our view that the product is highly selective to binding potassium. In addition to a potential cleaner side effect profile, ZS Pharma enrolled a broader patient population in the clinical trials, recruiting patients with hyperkalemia regardless of etiology. We also believe ZS-9 as a once-a-day maintenance therapy likely has an improved profile over patiromer in the large chronic dosing market.

- Although head-to-head studies of development compounds are rarely available and cross-trial comparison is always difficult because of different patient populations, we attempted to directionally compare the efficacy profiles of ZS-9 and patiromer in exhibit 5 (on page 5) using baseline and post-treatment mean serum potassium levels for patiromer studies using prior company reports. In the early-stage study comparison, at the 48-hour period, ZS-9 patients (especially at doses above 2.5 grams three times per day, or TID) are in the normokalemic range after treatment, whereas patiromer patients are still above the range (though significantly reduced from baseline) for normal potassium concentration. In addition, in the comparison of data after two weeks of treatment, ZS-9 in the maintenance phase showed lower mean serum potassium concentration (4.71 mEq/L for 5 g QD, and 4.55 mEq/L for 10 g QD), while our best estimate for 14-day data for

patiromer suggests end-values of 4.8 mEq/L for both the mild and moderate-to-severe hyperkalemia patients. We continue to believe that ZS-9 has a faster onset of action and a sustained benefit in comparison to patiromer.

- *Given the well-documented prevalence and growing patient populations within CKD, CHF, diabetes, and individuals on RAAS inhibitors, we believe the potential market for ZS-9 is significant and while we view it as the best-in-class agent, the large market may be able to still support patiromer if that product is approved.* Hyperkalemia is a life-threatening condition wherein elevated levels of potassium have been shown to increase the risk of ventricular fibrillation/cardiac arrest and death (Goyal et al. *JAMA* 2012). *In total, we believe the hyperkalemia market exceeds 3 million patients in the United States alone with few good treatment options.* 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. We view shares as our best near-term idea ahead of the readout of the HARMONIZE trial in late September/October.

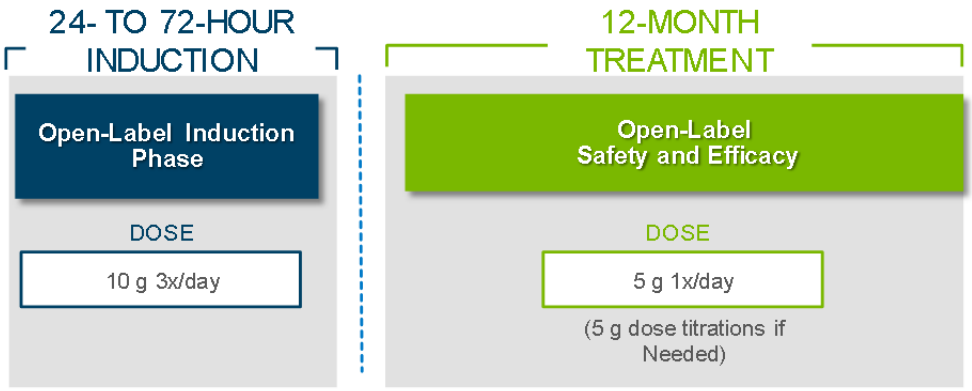
Exhibit 1
ZS Pharma, Inc.
HARMONIZE Study Design



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.
ZS005 Trial Design



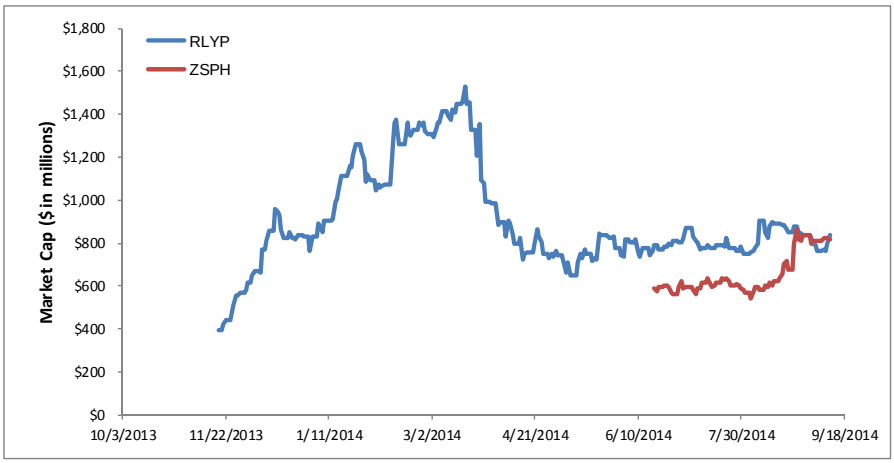
Primary Endpoint: Safety and tolerability over 12-month treatment period

Secondary Endpoints: Proportion of patients normokalemic after induction phase

Proportion of patients normokalemic during 12-month treatment period

Source: Company reports

Exhibit 3
ZS Pharma, Inc.
Comparison of ZSPH and RLYP Market Caps Since 2013



Source: FactSet, William Blair & Company, L.L.C.

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.

Exhibit 5
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	10g t.i.d	RLY5016-205 (AMETHYST-DN)	5.3 mEq/L ->4.71 mEq/L	5g q.d.	ZS-003
	Moderate/Severe HK ~5.6 mEq/L -> 4.8 mEq/L			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	Study Results in Q4 2014		ZS-004
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

Valuation

We rate shares of ZS-9 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 6). 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 6
ZS Pharma, Inc.
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					$ (2.41)
NPV Value					$ 1,807,728
NPV Value Per Share					$ 74.70

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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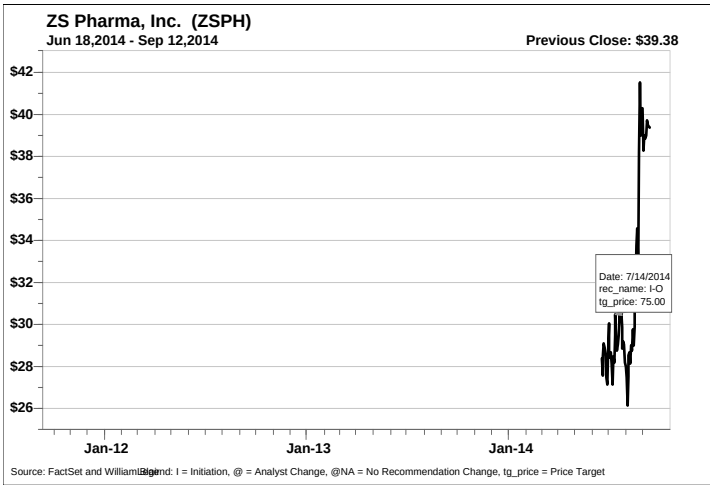
DOW JONES: 17,031.14
S&P 500: 1,984.13
NASDAQ: 4,518.90



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

*Percentage of companies in each rating category that are investment banking clients, defined as companies for which William Blair has received compensation for investment banking services within the past 12 months.

The compensation of the research analyst is based on a variety of factors, including performance of his or her stock recommendations; contributions to all of the firm's departments, including asset management, corporate finance, institutional sales, and retail brokerage; firm profitability; and competitive factors.

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