William Blair

March 13, 2015

Tim Lugo | +1 415 248 2870
tlugo@williamblair.com

Raju Prasad, Ph.D. | +1 312 364 8469
rprasad@williamblair.com

ZS Pharma, Inc.

Fourth-Quarter Earnings a Non-event; Long Term ZS-9 Data and NDA Filing in the Near Term with No Advisory Committee Expected

- Before the open on March 13, ZS Pharma reported fourth-quarter and full year 2014 results. Although earnings are a relative non-event for this development-stage company, the press release did have some important business development updates. Most notably, the company held a positive pre-NDA meeting with the FDA regarding ZS-9 and stated that patients are entering into their 11th month of therapy in the long-term trials. While we had previously questioned if there would be an advisory committee for either competitive program, Relypsa's (RLYP $40.38) patiromer or ZS-9, the FDA informed ZS Pharma that it does not plan to conduct one at this time. We believe this is due to the FDA's acknowledgement of the large market for hyperkalemia and unmet medical need, which we believe has been questioned in the past.

- ZS Pharma expects to file its NDA with the FDA in the second quarter (in line with previous guidance) and its MAA with the EMA in the second half of 2015. Additionally the company appointed Martin Babler to the board of directors, who brings commercial experience, having launched Xolair and Rituxan at Genentech. ZS Pharma also brought in key commercial personnel with experience from Genentech (RHHBY $32.84), Sanofi/Genzyme (SNY $47.18), and Amgen (AMGN $154.18; Market Perform) as the company lays the groundwork for the launch of ZS-9 in 2016.

- As we approach the filing of the ZS-9 NDA and the release of long-term safety data, we continue to believe ZS-9 will hold a best-in-class profile against patiromer. Patiromer has some benefits over ZS-9, namely being two quarters ahead to market and being a non-metal-based binder (which we believe is more of a Street issue than a significant marketing liability). Patiromer also holds an improved rate of edema, which Relypsa often notes in its press releases; however, we believe other issues with the patiromer dataset are more concerning than an edema rate in a dose (15g) that will likely be used by less than 5% of all patients. Overall, we believe patiromer's benefits are outweighed by what will likely be a superior long-term safety profile from ZS-9. Management today cited 11 months of treatment in its long-term safety study to date, and we continue to believe that 1-year mortality could be significantly lower than the 5% observed in the patiromer long-term study.

- While cross trial comparisons are always difficult, we note that patiromer may expose patients to a significant amount of calcium, which will likely be a marketing hindrance after years of anti-calcium binder messaging by Genzyme and Shire (SHPG $243.39; Outperform). As calcium-based binders still see significant utilization in the chronic kidney disease population, those physicians who prescribe them may not be comfortable to potentially double their calcium intake with 2.4 grams of calcium included in patiromer's mild HK dosing, let alone the "double-double" of calcium exposed to patients in the high HK patiromer dose (4 grams). KDOQI guidelines suggest total elemental calcium intake (including dietary calcium) should not exceed 2 grams, and while Relypsa describes the calcium as non-absorbed, we are unsure if that has been clinically validated. Regardless, the FDA is well aware of calcium-based binders, so the risk is likely not a question of approvability; however, it may be a marketing liability.

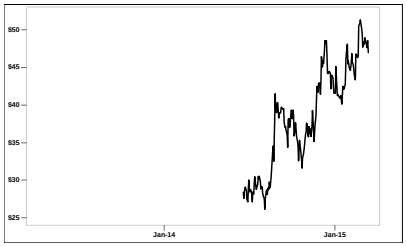
Stock Rating:	**Outperform**
Company Profile:	**Aggressive Growth**
Price Target:	$75.00
Symbol:	ZSPH (NASDAQ)
Price:	$47.23 (52-Wk.: $26-$53)
Market Value (mil.):	$991
Fiscal Year End:	December
Long-Term EPS Growth Rate:	
Dividend/Yield:	None

		2014A	2015E	2016E
Estimates				
EPS	Q1	$0.02	$-0.93	NA
	Q2	$-4.72	$-0.95	NA
	Q3	$-0.81	$-1.00	NA
	Q4	$-0.98	$-1.02	NA
	FY	$-5.47	$-3.90	$-3.84
	CY		$-3.90	$-3.84
Sales (mil.)		0	0	37
Valuation				
FY P/E		NM	NM	NM
CY P/E			NM	NM

Trading Data (FactSet)	
Shares Outstanding (mil.)	21
Float (mil.)	10
Average Daily Volume	192,137

Financial Data (FactSet)	
Long-Term Debt/Total Capital (MRQ)	0.0
Book Value Per Share (MRQ)	5.5
Return on Equity (TTM)	-235.2

Two-Year Price Performance Chart



Sources: FactSet, William Blair & Company estimates

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

- We continue to note the higher affinity for patiromer to bind magnesium versus potassium and the relatively high rate of hypomagnesemia in the company's PEARL-HF study (24%). It is also interesting to note the lower rates observed in OPAL-HK (3%-4%) versus PEARL-HF. A deeper look into the data suggests that a change in the definition of hypomagnesemia from the PEARL-HF study to the OPAL-HK study likely aided this decreased rate of hypomagnesemia, as shown in exhibit 1. Our review of the literature on hypomagnesemia suggests this 1.4mg/dL rate utilized in OPAL-HK is a relatively low threshold that was not utilized in any of the publications we reviewed. Although some have pointed to the National Institutes of Health Common Terminology Criteria for Adverse Events guidelines that suggest a 1.2 mg/dL definition of grade 1 hypomagnesemia, we cannot help but consider this issue when both products are potentially being marketed to nephrologists for chronic kidney disease patients when the KDOQI guidelines state that, "hypomagnesemia is defined as serum magnesium <1.8 mEq/L". We also note that it is stated in the guidelines that "serum magnesium is a poor indicator of quantitative deficiency unless values below 1 mEq/L are present"; however, in Relypsa's AMETHYST-RN data, hypomagnesemia was determined by the PI and not lab values. We expect to learn more about this issue and hear some additional feedback from the physician community during the upcoming NKF Spring Clinical Meetings in Dallas from March 25-29, where both companies will have a presence.

- Regarding fourth-quarter financials, the company reported a net loss of $20.3 million, or a loss of $0.98 per share, which was below our estimate of $17 million or $0.81 per share and consensus of $14.8 million or $0.75 per share. R&D and G&A costs were $14.6 million and $5.5 million, respectively, that represented 33% and -3% growth quarter-over-quarter in the company's second full quarter as a public company. We show reported results and our estimates in exhibit 2.

- We continue to rate shares of ZS Pharma Outperform with a price target of $75, based on our belief that ZS-9 holds a best-in-class profile for the treatment of hyperkalemia. In total, we believe the acute and chronic hyperkalemia market exceeds 3 million patients in the U.S. and has been reported in up to 10% of all hospitalized patients with few good treatment options. While we believe the market may be large enough for two winners, we ultimately view the profile of ZS-9 as the likely best-in-class product, and we believe long-term safety data, which should be available later in the year at an appropriate medical meeting, will likely cement that profile. The next meaningful catalysts for ZS Pharma will likely be the filing of the ZS-9 NDA, which may occur in the near term. We continue to view ZS Pharma as a best pick in 2015.

Exhibit 1
Definition of Hypomagnesemia in PEARL-HF and OPAL-HK (Replysa Clinical Trials) and Reported Events

	PEARL-HF	OPAL-HK
Hypomagnesemia Definition	serum Mg2+ <1.8 mg/dL	serum Mg2+ <1.4 mg/dL
Rate of Hypomagnesemia reported	24% of patients treated with patiromer vs. 2.1% in placebo, statistically significant decrease from baseline was observed (-0.22 vs. 0.01 mg/dL for the patiromer and placebo groups respectively, P<0.001)	A serum magnesium level of less than 1.4 mg per deciliter (0.58 mmol per liter) occurred in eight patients (3%) during the initial treatment phase and through its follow-up period. Magnesium-replacement therapy was initiated in nine patients (4%) in the patiromer group during the initial treatment phase.

Sources: Pitt et al. Eur Heart J 2011, Weir et al. NEJM 2014

Exhibit 2
ZS Pharma
Fourth Quarter Results and Estimates

	ZSPH Q4 14A	WB Q4 14E	Consensus Q4 14E	Q/Q Growth	Y/Y Growth
($ in thousands except EPS)					
Total Revenue	**$ -**	**$ -**	**$ -**	**NA**	**NA**
R&D	$ 14,574.0	$ 11,000.0	$ 18,300.0	33%	112%
G&A	$ 5,535.0	$ 5,500.0	$ 9,700.0	-3%	57%
Operating Income (loss)	$ (20,109.0)	$ (16,500.0)	$ (27,700.0)	NM	NM
Net Income (loss)	$ (20,315.0)	$ (17,025.0)	$ (14,800.0)	NM	NM
EPS	**$ (0.98)**	**$ (0.81)**	**$ (0.75)**	**NM**	**NM**

Source: Company reports, William Blair & Company L.L.C. estimates
Consensus estimates reported by FactSet

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. 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.

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

William Blair

ZS Pharma
Earnings Model
3/13/15
($ in millions except EPS data)

Rating: Outperform
Company Profile: Aggressive Growth
Tim Lugo
415.248.2870
tlugo@williamblair.com

	2012(A)	2013(A)	2014(A)	Q1(E)	Q2(E)	Q3(E)	Q4(E)	2015(E)	2016(E)	2017(E)	2018(E)	2019(E)
ZS-9	-	-	-	-	-	-	-	-	36,767	218,357	445,814	740,445
Royalty/Milestone Revenue	-	-	-	-	-	-	-	-	-	-	-	-
Total Revenue	-	-	-	-	-	-	-	-	36,767	218,357	445,814	740,445
yr/yr growth	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	104.2%	66.1%
q/q growth				NA	NA	NA	NA					
incremental rev q/q												
Cost of Goods Sold	-	-	-	-	-	-	-	-	3,677	21,836	44,581	74,044
Gross Profit	-	-	-	-	-	-	-	-	33,090	196,521	401,233	666,400
SG&A	1,148	7,686	14,919	5,000	5,500	5,500	6,000	22,000	44,000	88,000	102,537	148,089
Growth			30%					20%	100%	100%	76%	15%
R&D	6,989	24,508	45,618	14,000	14,000	15,000	15,000	58,000	69,600	80,040	88,044	92,446
Growth		251%	86%	-	-	-	-	20%	20%	15%	10%	5%
Total Operating Expenses	8,137	32,194	60,537	19,000	19,500	20,500	21,000	80,000	113,600	168,040	190,581	240,535
growth			88%	676%	34%	23%	4%	32%	42%	48%	13%	26%
Operating Income	(8,137)	(32,194)	(60,537)	(19,000)	(19,500)	(20,500)	(21,000)	(80,000)	(80,510)	28,481	210,651	425,865
EBIT Margin			NM					NM	NM	NM	47%	58%
growth y/y (%)			NM	676%	34%	23%	4%	NM	NM	NM	NM	NM
Depreciation and Amortization	-		1,000	250	250	250	250	1,000	1,000	1,000	1,000	1,000
EBITDA	(8,137)	(32,194)	(59,537.0)	(18,750)	(19,250)	(20,250)	(20,750)	(79,000.0)	(79,509.7)	29,481	211,651	426,865
			NM					NM	NM	NM	47%	58%
Interest income	(17)	(31)	(94)	225.0	200.0	175.0	150.0	750	600	800	1,200	1,400
Interest expense	2,099	9	530	500	500.0	500.0	500.0	2,000	1,500	1,500	1,000	1,000
Change in fair value of warrants	62	1,424	3,071.0									
Other	-	1										
Income Before Taxes	(10,281)	(33,597)	(64,044)	(19,275)	(19,800)	(20,825)	(21,350)	(81,250)	(81,410)	27,781	210,851	426,265
Income Tax Provision	-	-		250	250	250	250	1,000	1,000	10,001	71,689	144,930
Effective Tax Rate	0.0%	0.0%	NM	-1.3%	-1.3%	-1.2%	-1.2%	NA	NA	34%	34%	34%
Preferred stock accretion	(174)	(689)	(310)									
Net Income (loss) Attributable to Common	(10,455)	(34,286)	(64,354)	(19,525)	(20,050)	(21,075)	(21,600)	(82,250)	(82,410)	17,780	139,162	281,335
Net loss per share (diluted)	$ (2.63)	$ (8.52)	$ (5.47)	(0.93)	(0.95)	(1.00)	(1.02)	$ (3.90)	$ (3.84)	$ 0.81	$ 6.33	$ 12.49
Basic avg. number of shares used in computing net income	3,981	4,025	11,768	20,932	21,032	21,132	21,232	21,082	21,482	21,882	21,682	21,682
Diluted avg. number of shares used in computing net income	3,981	4,025	11,768	20,932	21,032	21,132	21,232	21,082	21,482	21,882	21,982	22,526
Key Ratios (GAAP unless noted)												
Gross Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	90.0%	90.0%	90.0%
R&D (% Total Rev.)	NM	NM	NM	NM	NM	NM	NM	NM	NM	36.7%	19.7%	12.5%
SG&A (% Total Rev.)	NM	NM	NM	NM	NM	NM	NM	NM	NM	40.3%	**23.0%**	**20.0%**
Operating Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	13.0%	47.3%	57.5%
Net Income Margin	NM	NM	NM	NM	NM	NM	NM	NM	NM	8.1%	31.2%	38.0%
Revenue Growth												
Growth Yr/Yr	NM	NM	NM	NM	NM	NM	NM	NM	NM	494%	104%	66%
Growth Q/Q	NM			NM	NM	NM	NM					
SG&A Growth												
Growth Yr/Yr	NM	570%	94%	375%	21%	-3%	8%	47%	100%	100%	17%	44%
Growth Q/Q	NM			-10%	10%	0%	9%					
R&D Growth												
Growth Yr/Yr	NM	251%	86%	904%	40%	37%	3%	27%	20%	15%	10%	5%
Growth Q/Q	NM			-4%	0%	7%	0%					

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.

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.

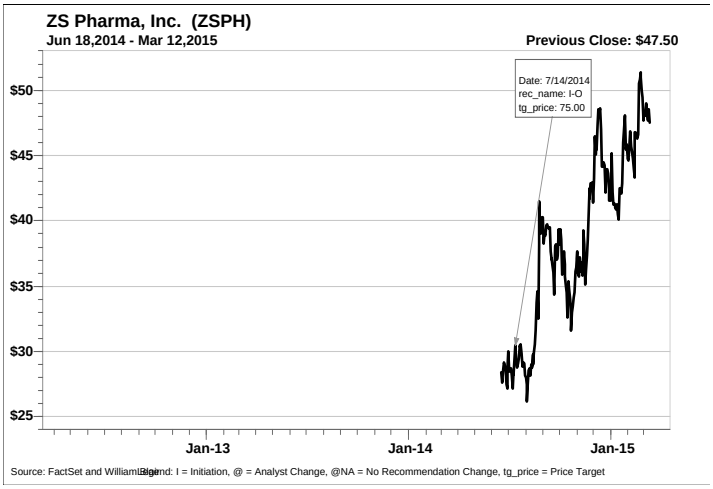
Additional information is available upon request.

This report is available in electronic form to registered users via R*Docs™ at www.rdocs.com or www.williamblair.com.

Please contact us at +1 800 621 0687 or consult williamblair.com/Research-and-Insights/Equity-Research/Coverage.aspx for all disclosures.

Tim Lugo attests that 1) all of the views expressed in this research report accurately reflect his/her personal views about any and all of the securities and companies covered by this report, and 2) no part of his/her compensation was, is, or will be related, directly or indirectly, to the specific recommendations or views expressed by him/her in this report. We seek to update our research as appropriate, but various regulations may prohibit us from doing so. Other than certain periodical industry reports, the majority of reports are published at irregular intervals as deemed appropriate by the analyst.

DOW JONES: 17,895.22
S&P 500: 2,065.95
NASDAQ: 4,893.29



Current Rating Distribution (as of 02/28/15)

Coverage Universe	Percent	Inv. Banking Relationships*	Percent
Outperform (Buy)	65	Outperform (Buy)	16
Market Perform (Hold)	32	Market Perform (Hold)	2
Underperform (Sell)	2	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.

OTHER IMPORTANT DISCLOSURES

Stock ratings, price targets, and valuation methodologies: William Blair & Company, L.L.C. uses a three-point system to rate stocks. Individual ratings and price targets (where used) reflect the expected performance of the stock relative to the broader market (generally the S&P 500, unless otherwise indicated) over the next 12 months. The assessment of expected performance is a function of near-, intermediate-, and long-term company fundamentals, industry outlook, confidence in earnings estimates, valuation (and our valuation methodology), and other factors. Outperform (O) – stock expected to outperform the broader market over the next 12 months; Market Perform (M) – stock expected to perform approximately in line with the broader market over the next 12 months; Underperform (U) – stock expected to underperform the broader market over the next 12 months; not rated (NR) – the stock is not currently rated. The valuation methodologies used to determine price targets (where used) include (but are not limited to) price-to-earnings multiple (P/E), relative P/E (compared with the relevant market), P/E-to-growth-rate (PEG) ratio, market capitalization/revenue multiple, enterprise value/EBITDA ratio, discounted cash flow, and others.

Company Profile: The William Blair research philosophy is focused on quality growth companies. Growth companies by their nature tend to be more volatile than the overall stock market. Company profile is a fundamental assessment, over a longer-term horizon, of the business risk of the company relative to the broader William Blair universe. Factors assessed include: 1) durability and strength of franchise (management strength and track record, market leadership, distinctive capabilities); 2) financial profile (earnings growth rate/consistency, cash flow generation, return on investment, balance sheet, accounting); 3) other factors such as sector or industry conditions, economic environment, confidence in long-term growth prospects, etc. Established Growth (E) – Fundamental risk is lower relative to the broader William Blair universe; Core Growth (C) – Fundamental risk is approximately in line with the broader William Blair universe; Aggressive Growth (A) – Fundamental risk is higher relative to the broader William Blair universe.

The ratings, price targets (where used), valuation methodologies, and company profile assessments reflect the opinion of the individual analyst and are subject to change at any time.

Our salespeople, traders, and other professionals may provide oral or written market commentary or trading strategies—to our clients and our trading desks—that are contrary to opinions expressed in this research. Certain outstanding reports may contain discussions or investment opinions relating to securities, financial instruments and/or issuers that are no longer current. Always refer to the most recent report on a company or issuer before making an investment decision. Our asset management and trading desks may make investment decisions that are inconsistent with recommendations or views expressed in this report. We will from time to time have long or short positions in, act as principal in, and buy or sell the securities referred to in this report. Our research is disseminated primarily electronically, and in some instances in printed form. Electronic research is simultaneously available to all clients. This research is for our clients only. No part of this material may be copied or duplicated in any form by any means or redistributed without the prior written consent of William Blair & Company, L.L.C.

This is not in any sense a solicitation or offer of the purchase or sale of securities. The factual statements herein have been take from sources we believe to be reliable, but such statements are made without any representation as to accuracy or completeness or otherwise. Opinions expressed are our own unless otherwise stated. Prices shown are approximate.

This material is distributed in the United Kingdom and the European Economic Area (EEA) by William Blair International, Ltd., authorized and regulated by the Financial Conduct Authority (FCA), and is only directed at and is only made available to persons falling within articles 19, 38, 47, and 49 of the Financial Services and Markets Act of 2000 (Financial Promotion) Order 2005 (all such persons being referred to as "relevant persons"). This document is intended for persons regarded as professional investors (or equivalent) and is not to be distributed to or passed onto any "retail clients." No persons other than persons to whom this document is directed should rely on it or its contents or use it as the basis to make an investment decision.