

June 10, 2015

## ZS Pharma, Inc.

### Highlights From William Blair's 35th Annual Growth Stock Conference

- On Tuesday, June 9, ZS Pharma's Chief Executive Officer Robert Alexander presented at our annual growth stock conference. The company has made significant clinical and regulatory advancements since becoming a public company in 2014. The most recent advancement being the NDA filing of its lead candidate ZS-9 to treat hyperkalemia or increased serum potassium concentrations (above the normal range of 3.5 mEq/L to 5.0 mEq/L), which is associated with morbidity and mortality. At the conference, management highlighted the vast clinical program for ZS-9, which includes a positive Phase II trial and two positive Phase III trials that have tested the product in over 1,000 patients (exhibit 1). The company has two ongoing long-term studies, ZS004e, an 11-month extension study of its second Phase III trial HARMONIZE, and ZS005, a 12-month open-label safety study in 750 patients that was initiated in second quarter 2014. The company anticipates announcing data in the second half of 2015, and we note the 120-day safety submission (assuming NDA acceptance in July) is in September/October.
- Several investor questions focused on the potential pricing of chronic hyperkalemia therapies. Management noted that payers are using the phosphate binder market as a model, with sevelamer pricing in the \$700-\$1,000/month range for private insurance. Furthermore, to properly gauge the market potential for hyperkalemia, the company noted that phosphate binders are primarily used for end-stage renal disease (400,000-500,000 patients) versus hyperkalemia, which is estimated to impact 3 million-4 million patients with an estimated 50% of the market private pay versus Medicare part D.
- We continue to believe that ZS-9 has a best-in-class profile, with a differentiated onset of action that has shown a median time to K<sup>+</sup> normalization in 2.2 hours, 84% of patients normalized by 24 hours and 98% of patients normalized by 48 hours. A significant proportion of patients saw normalization of potassium levels up to 4 weeks of maintenance therapy with ZS-9 compared to placebo in HARMONIZE. According to market research previously presented by the company, a large proportion of physicians would use a new K<sup>+</sup> binder to provide RAAS therapy to patients that have hyperkalemia (exhibit 2). Furthermore, clinicians would use a new K<sup>+</sup> binder in a large proportion of patients with 5.5 mEq/L or higher serum K<sup>+</sup> concentrations (exhibit 3).
- Regarding the safety profile of ZS-9, gastrointestinal adverse events were comparable to placebo levels with no drug-related serious adverse events. Additionally, there were no clinically significant changes in other ions (sodium, magnesium, and calcium) and no significant hypokalemia (serum K<sup>+</sup> <3.0 mEq/L). Edema, which was a concern after the HARMONIZE data readout, is believed to be lower than the placebo arm rate in prior studies after the company took a recent look at the ongoing long-term safety studies. The company anticipates releasing the full data set from the long-term studies in the second half of the year, which we believe could be a catalyst for shares.

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

Please consult pages 4-5 of this report for all disclosures. Analyst certification is on page 4. William Blair or an affiliate does and seeks to do business with companies covered in its research reports. As a result, investors should be aware that the firm may have a conflict of interest that could affect the objectivity of this report. Investors should consider this report as a single factor in making an investment decision.

*William Blair*

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

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

Stock Rating: **Outperform**  
Company Profile: **Aggressive Growth**  
Price Target: **\$75.00**

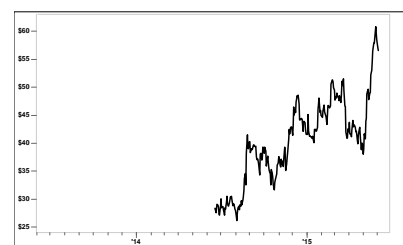
Symbol: ZSPH (NASDAQ)  
Price: \$56.11 (52-Wk.: \$26-\$63)  
Market Value (mil.): \$1,412  
Fiscal Year End: December  
Long-Term EPS Growth Rate:  
Dividend/Yield: None

	2014A	2015E	2016E
<b>Estimates</b>			
EPS Q1	\$0.02	A\$-1.05	NA
Q2	\$-4.72	\$-0.95	NA
Q3	\$-0.81	\$-0.99	NA
Q4	\$-0.98	\$-1.01	NA
FY	\$-5.47	\$-4.01	\$-4.17
CY		\$-4.01	\$-4.17
Sales (mil.)	0	0	37
<b>Valuation</b>			
FY P/E	NM	NM	NM
CY P/E		NM	NM

<b>Trading Data (FactSet)</b>	
Shares Outstanding (mil.)	21
Float (mil.)	9
Average Daily Volume	309,009

<b>Financial Data (FactSet)</b>	
Book Value Per Share (MRQ)	10.1
Return on Equity (TTM)	-124.1

### Two-Year Price Performance Chart



Sources: FactSet, William Blair & Company estimates

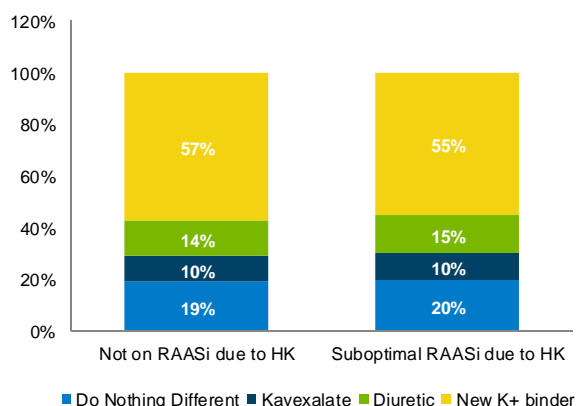
- Recall that competitive product patiomer has a PDUFA date of October 21 for its BID formulation, and the likelihood of an early 2016 full launch of the product (which will put them several months ahead of a ZS-9 launch). Given the significant market opportunity and the need for both companies to build awareness in the chronic setting, we believe having two marketers of the product will likely be a positive for the class. Management continues to believe the company will file the MAA for ZS-9 in the fourth quarter. We note that both Relypsa (RLYP \$34.64) and ZS Pharma continue to believe the FDA will not convene an Advisory Committee, which is likely a positive signal regarding the review of both NDAs and likely highlights the agency's desire for the approval of new therapies for hyperkalemia. Recall that the current standard of care, sodium polystyrene sulfonate (SPS), predates the modern FDA approval process. We also note that Ardelyx (ARDX \$14.61) recently announced that it is pursuing an accelerated 505(b)(2) pathway for RDX022, a non-absorbed polystyrene sulfonate polymer with improved chemical and formulation properties, for the treatment of hyperkalemia. The company plans to begin clinical trials in the near term, with a Phase III clinical trial beginning as early as the second half of 2016. The company has completed some preclinical work on RDX022 and plans to disclose more information on this product at its R&D day in July. We will see how the data compares with patiomer and ZS-9.
- We continue to believe that ZS-9 holds a best-in-class profile for the treatment of hyperkalemia and continue to rate shares of ZS Pharma Outperform with a price target of \$75. In total, we believe the acute and chronic hyperkalemia market exceeds 3 million patients in the United States 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, will likely cement that profile. To date we believe ZS-9 has shown to hold a faster onset of action, is efficacious across multiple subgroups, and will likely hold a strong long-term safety profile. We continue to view ZS Pharma as a top idea in 2015.

**Exhibit 1**  
**ZS Pharma, Inc.**  
**ZS-9 Development Program Overview**

Trial	Patient Population	Duration	Objective	Summary
ZS002 (Completed)	N=90 Hyperkalemia, CKD 5-6 mEq/L	48 hours	POC for ZS-9 rapidly lowering K+ levels	Met primary endpoint
ZS003 (Completed)	N=753 Hyperkalemia, regardless of etiology 5-6 mEq/L	14 days	Confirm rapid K+ control and POC for extended dosing	Met primary endpoint for the 2.5, 5, 10 doses and secondary endpoints for 5 and 10 dose in extended phase
ZS004/e (Completed/Ongoing)	N=258 Hyperkalemia, regardless of etiology. >5 mEq/L	1 month + 11 month	Establish an extended dose	80%, 90%, and 94% normokalemic at 5g, 10g, and 15g QD doses, respectively
ZS005 (Ongoing)	N=500 Hyperkalemia, regardless of etiology. >5 mEq/L	12 months	Establishing long-term safety and efficacy	Initiated 2Q14; Data available in 2H '15

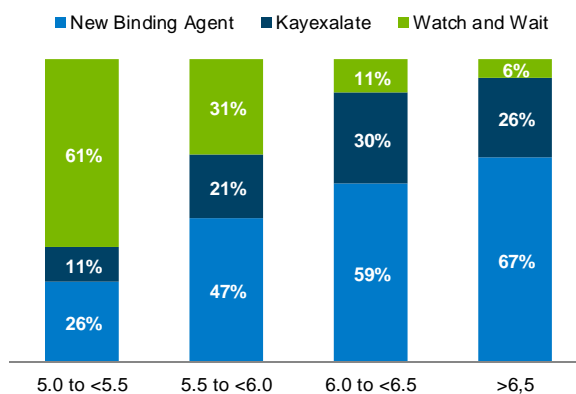
Source: Company reports

**Exhibit 2**  
**Physician Sentiment On Use Of K<sup>+</sup> Binders to Enable Optimal RAASi Therapy**



Source: Company reports

**Exhibit 3**  
**ZS Pharma Market Research On Potential Utilization Of K<sup>+</sup> Binders Stratified by Serum Concentration**



Source: 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. 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.

### **IMPORTANT DISCLOSURES**

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

William Blair or an affiliate is a market maker in the security of ZS Pharma, Inc.

William Blair or an affiliate expects to receive or intends to seek compensation for investment banking services from ZS Pharma, Inc. within the next three months.

William Blair or an affiliate received compensation for investment banking services from ZS Pharma, Inc. within the last 12 months. ZS Pharma, Inc. is or was, within the last 12 months, an investment banking client of William Blair & Company and/or one or more of its affiliates.

Additional information is available upon request.

This report is available in electronic form to registered users via R\*Docs™ at [www.rdocs.com](http://www.rdocs.com) or [www.williamblair.com](http://www.williamblair.com).

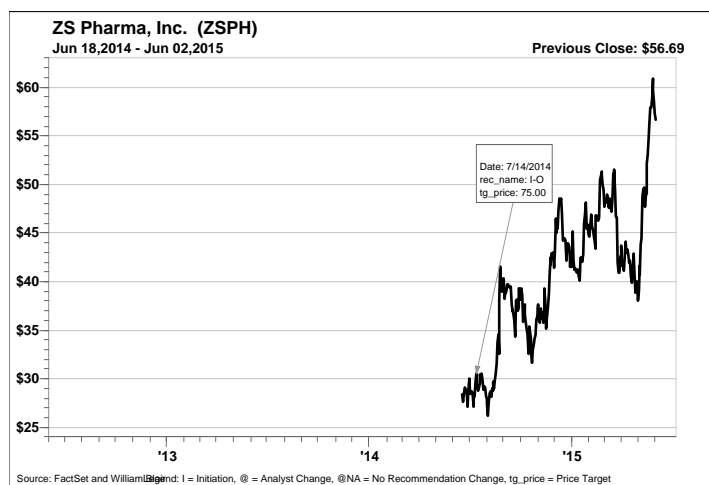
Please contact us at +1 800 621 0687 or consult [williamblair.com/Research-and-Insights/Equity-Research/Coverage.aspx](http://williamblair.com/Research-and-Insights/Equity-Research/Coverage.aspx) for all disclosures.

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: 17,764.04

S&P 500: 2,080.15

NASDAQ: 5,013.86



### **Current Rating Distribution (as of 05/31/15)**

Coverage Universe	Percent	Inv. Banking Relationships*	Percent
Outperform (Buy)	65	Outperform (Buy)	14
Market Perform (Hold)	33	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.

#### **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 taken 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.

“William Blair” and “R\*Docs” are registered trademarks of William Blair & Company, L.L.C. Copyright 2015, William Blair & Company, L.L.C. All rights reserved.