Acquisition of ZS Pharma

Conference call  6 November 2015
Forward-looking statements

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Forward-looking statements continued

Some of the statements contained in this announcement are forward-looking statements, including statements regarding the expected consummation of the acquisition, which involves a number of risks and uncertainties, including the satisfaction of closing conditions for the acquisition, such as regulatory approval for the transaction, the tender of a majority of the outstanding shares of common stock of ZS Pharma, the possibility that the transaction will not be completed and other risks and uncertainties discussed in ZS Pharma's public filings with the United States Securities and Exchange Commission (SEC), including the “Risk Factors” sections of ZS Pharma's Annual Report on Form 10-K for the year ended December 31, 2014 and subsequent quarterly reports on Form 10-Q, as well as the tender offer documents to be filed by subsidiaries of AstraZeneca and the solicitation/recommendation to be filed by ZS Pharma. These statements are based on current expectations, assumptions, estimates and projections, and involve known and unknown risks, uncertainties and other factors that may cause results, levels of activity, performance or achievements to be materially different from any future statements. These statements are generally identified by words of phrases such as “believe”, “anticipate”, “expect”, “intend”, “plan”, “will”, “may”, “should”, “estimate”, “predict”, “potential”, “continue” or the negative of such terms or other similar expressions. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialise, actual results and the timing of events may differ materially from the results and/or timing discussed in the forward-looking statements, and you should not place undue reliance on these statements. AstraZeneca and ZS Pharma disclaim any intent or obligation to update any forward-looking statements as a result of developments occurring after the date hereof or otherwise.

Additional information and where to find it

These materials are for informational purposes only and does not constitute an offer to purchase or a solicitation of an offer to sell ZS Pharma common stock. The offer to buy ZS Pharma common stock will only be made pursuant to a tender offer statement (including the offer to purchase, letter of transmittal and other related tender offer materials). Investors and security holders are urged to read both the tender offer statement (which will be filed by subsidiaries of AstraZeneca with the Securities and Exchange Commission (SEC)) and the solicitation/recommendation statement on schedule 14D-9 with respect to the tender offer (which will be filed by ZS Pharma with the SEC) when they become available because they will contain important information, including the terms and conditions of the offer. Investors and security holders may obtain a free copy of these materials (when available) and other documents filed by AstraZeneca and ZS Pharma with the SEC at the website maintained by the SEC at www.sec.gov. The tender offer statement and related materials, and the solicitation/recommendation statement, may also be obtained (when available) for free by contacting AstraZeneca Investor Relations at irteam@astrazeneca.com.

Copies of these materials and any documents relating to the tender offer are not being, and must not be, directly or indirectly, mailed or otherwise forwarded, distributed or sent in, into or from any jurisdiction where to do so would be unlawful.
# Agenda

<table>
<thead>
<tr>
<th>Section</th>
<th>Presenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overview</td>
<td>Pascal Soriot</td>
</tr>
<tr>
<td>Opportunity</td>
<td>Luke Miels</td>
</tr>
<tr>
<td>Clinical</td>
<td>Sean Bohen</td>
</tr>
<tr>
<td>Terms</td>
<td>Marc Dunoyer</td>
</tr>
<tr>
<td>Summary</td>
<td>Pascal Soriot</td>
</tr>
</tbody>
</table>
Overview

**Strengthens focus in Cardiovascular & Metabolic Disease**
- Adds ZS-9, potential best-in-class specialty treatment
- Leverages roxadustat and Diabetes franchise

**Hyperkalaemia can be a life-threatening condition**
- Chronic kidney disease (CKD) and chronic heart failure (CHF) with increasing prevalence
- Limited alternative treatment options, current and near term

>3 million patients with hyperkalaemia in the US

Global potential peak-year sales >$1bn

**Transaction supports Return to Growth strategy**
- Anticipated Product Sales from 2016; PDUFA date: 26 May 2016
- Expected growth in all regions, including Emerging Markets

Core EPS-accretive from 2018; marginally dilutive in 2016 & 2017
Cardiovascular & Metabolic Disease strategy

Reducing cardiovascular morbidity, mortality and organ damage by addressing multiple risk factors

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>Metabolism</th>
<th>CKD</th>
</tr>
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<tbody>
<tr>
<td><img src="image1.png" alt="Heart Icon" /></td>
<td><img src="image2.png" alt="Stomach Icon" /></td>
<td><img src="image3.png" alt="Kidneys Icon" /></td>
</tr>
</tbody>
</table>

- ZS-9 cardio-renal opportunity with potential launch in 2016
- Leverages roxadustat and Diabetes franchise
About ZS Pharma

• Publicly traded (NASDAQ: ZSPH)

• Founded in 2008; headquartered in San Mateo, California

• Development manufacturing site in Coppell, Texas

• ~200 employees

• Strong expertise, know-how and capabilities in CKD

• Net cash position
Hyperkalaemia is a leading cause of mortality in CKD

Odds ratio of death within 24hr period after hyperkalaemia

K+ level, mEq/L
- <5.5
- ≥5.5 & ≤6.0
- >6.0

## CKD prevalence in key markets

<table>
<thead>
<tr>
<th>Region</th>
<th>Total CKD Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>27m</td>
</tr>
<tr>
<td>EU5</td>
<td>29m</td>
</tr>
<tr>
<td>JPN</td>
<td>14m</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage</th>
<th>US: 27m</th>
<th>EU5: 29m</th>
<th>JPN: 14m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>6.6m</td>
<td>3.9m</td>
<td>2.1m</td>
</tr>
<tr>
<td>Stage 2</td>
<td>6.0m</td>
<td>5.5m</td>
<td>4.9m</td>
</tr>
<tr>
<td>Stage 3</td>
<td>12.7m</td>
<td>18.1m</td>
<td>6.3m</td>
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<tr>
<td>Stage 4</td>
<td>701k</td>
<td>943k</td>
<td>515k</td>
</tr>
<tr>
<td>Stage 5</td>
<td>645k</td>
<td>365k</td>
<td>343k</td>
</tr>
</tbody>
</table>

*Source: Decision Resources Group, Chronic Kidney Disease Patient Base, May 2015*
Management of hyperkalaemia in chronic kidney disease

Csaba P. Kovesdy

Abstract | Hyperkalaemia is common in patients with chronic kidney disease (CKD), in part because of the effects of kidney dysfunction on potassium homeostasis and in part because of the cluster of comorbidities (and their associated treatments) that occur in patients with CKD. Owing to its electrophysiological effects, severe hyperkalaemia represents a medical emergency that usually requires prompt intervention, whereas the prevention of hazardous hyperkalaemic episodes in at-risk patients requires measures aimed at the long-term normalization of potassium homeostasis. The options for effective and safe medical interventions to restore chronic potassium balance are few, and long-term management of hyperkalaemia is primarily limited to the correction of modifiable exacerbating factors. This situation can result in a difficult trade-off in patients

“The medications linked to hyperkalaemia that are most relevant are RAAS inhibitors (ACE inhibitors, ARBs, direct renin inhibitors and mineralocorticoid-receptor blockers).”

“Maintaining the use of these beneficial medications while implementing various strategies to control potassium balance is desirable; however, discontinuation rates remain high.”

Source: Kovesdy, C.P. Nat. Rev. Nephrol. 10, 653-662 (2014); published online 16 September 2014; doi:10.1038/nrneph.2014.168
Causes of hyperkalaemia in CKD/CHF

Those with chronic disease ...

Affected by HK\(^1\)

- **20 – 50%**
  - CKD

- **Up to 20%**
  - CHF

... and on lifesaving RAASi therapies

ACEs, ARBs and aldosterone antagonists

High K\(^+\) cited by nephrologists and cardiologists as key reason for under utilising RAASi therapy in CHF and CKD

Limited alternative treatment options

<table>
<thead>
<tr>
<th>K+ level (mEq/L)</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.0</td>
<td>Titrate RAASi, adjust diet</td>
<td>Titrate RAASi, adjust diet, +/- kayexalate</td>
<td>Discontinue RAASi, +/- emergency measures</td>
</tr>
<tr>
<td>5.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Current treatment options**

- **Phase I, II, III: 0**
- **Submitted:** ZS-9
- **Approved:** patiromer
- **Marketed:** kayexalate

**Source:** Company data, Morgan Stanley research
ZS-9: Potential best-in-class treatment for hyperkalaemia

- Proprietary zirconium silicate compound
- Non-systemically absorbed
- Odourless, tasteless 5-15g once a day
- Onset of action ~2hrs
- No significant drug-drug interaction
- Long-term stability at room temperature
- Pending and granted patents with expiries out to 2032 and beyond
### ZS-9: ~1,700 patients in clinical development programme

<table>
<thead>
<tr>
<th>Trial</th>
<th>Published</th>
<th>Trial type</th>
<th># Patients</th>
<th>Duration</th>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZS002</td>
<td></td>
<td>Phase II</td>
<td>N=90</td>
<td>48 hours</td>
<td>Δ serum K+ level (3 doses)</td>
</tr>
<tr>
<td>(Completed)</td>
<td></td>
<td>Double-blind</td>
<td>Serum K</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>RCT</td>
<td>5.0–6.0 mEq/L</td>
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<tr>
<td>ZS003</td>
<td></td>
<td>Phase III</td>
<td>N=753</td>
<td>14 days</td>
<td>Δ serum K+ level (4 doses)</td>
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<tr>
<td>(Completed)</td>
<td></td>
<td>Double-blind</td>
<td>Serum K</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RCT</td>
<td>5.0–6.5 mEq/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZS004e</td>
<td></td>
<td>Phase III</td>
<td>N=258</td>
<td>1 month +</td>
<td>Maintenance of serum K+</td>
</tr>
<tr>
<td>(Completed/extension ongoing)</td>
<td></td>
<td>Double-blind</td>
<td>Serum K</td>
<td>11 month</td>
<td>(28 days)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RCT</td>
<td>&gt;5.0 mEq/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZS005</td>
<td></td>
<td>Open-label safety</td>
<td>N=750</td>
<td>12 months</td>
<td>Safety &amp; tolerability of long-term dose (initiated Q2 2014)</td>
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<tr>
<td>(Ongoing)</td>
<td></td>
<td>trial</td>
<td>Serum K</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;5.0 mEq/L</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ZS-9: Efficacy summary

- All trials met primary endpoints
- Trials in CKD, CHF, diabetic patients
- Reduction in aldosterone
- Increase in bicarbonate levels

ZS-9: Safety and tolerability summary

• Gastrointestinal adverse-event rates comparable to placebo (<1%)

• No clinically-significant changes in sodium, magnesium or calcium levels

• Few hypokalaemia cases below 3.0mEq/L

• Peripheral oedema 1.0% (<2.5g), 0.0% (5g), 4.4% (10g), 10.7% (15g) and 1.7% (placebo)¹

Source: 1. Company due diligence. Treatment-emergent adverse events reported by >2.0% of subjects in any treatment group (safety population; completed trial ZS-003 and ZS-004)
Transaction terms

- Upon completion ZS Pharma will become a wholly-owned subsidiary
- All-cash transaction to acquire all of the outstanding capital stock of ZS Pharma for $90 per share; approximately $2.7 billion in aggregate transaction value
- Merger in which each remaining untendered share of ZS Pharma common stock would be converted into the same $90 per share cash consideration as in the tender offer
- Subject to the tender of a majority of the outstanding shares of ZS Pharma common stock and other and customary conditions
- Transaction expected to close this year
- Financed with a combination of cash and debt
- Acquisition accounted for as business combination
Summary

- Strengthens focus in Cardiovascular & Metabolic Disease
- Hyperkalaemia can be a life-threatening condition
- >3 million patients with hyperkaleamia in the US
- Global potential peak-year sales >$1bn
- Transaction supports Return to Growth strategy
- Core EPS-accrretive from 2018; marginally dilutive in 2016 & 2017
Questions