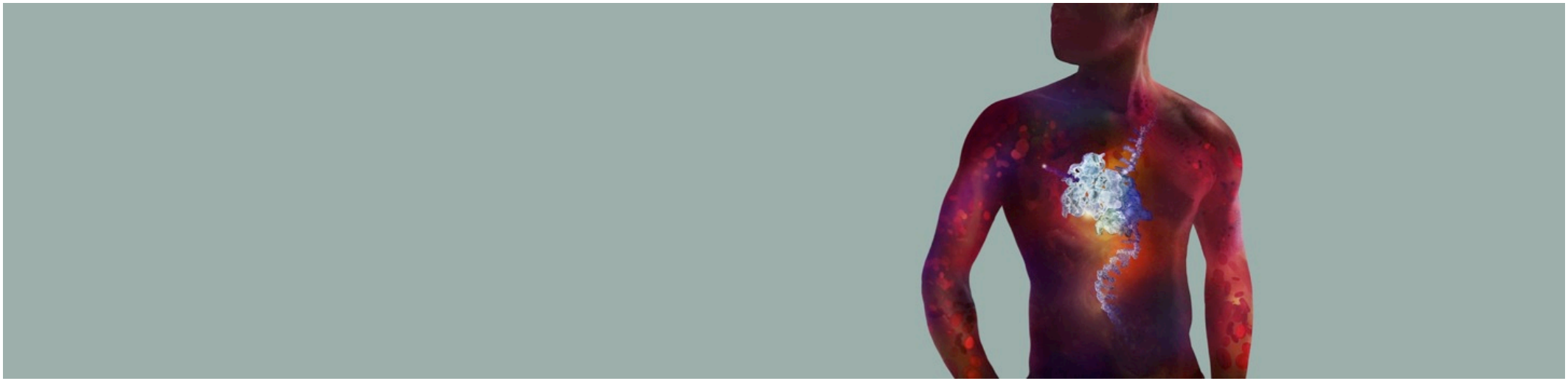
AstraZeneca
What science can do

# Acquisition of ZS Pharma

**Conference call**

**6 November 2015**



# Forward-looking statements

This document contains certain forward-looking statements with respect to the operations, performance and financial condition of the Group, including, among other things, statements about expected revenues, margins, earnings per share or other financial or other measures. Although we believe our expectations are based on reasonable assumptions, any forward-looking statements, by their very nature, involve risks and uncertainties and may be influenced by factors that could cause actual outcomes and results to be materially different from those predicted. The forward-looking statements reflect knowledge and information available at the date of preparation of this document and AstraZeneca undertakes no obligation to update these forward-looking statements. We identify the forward-looking statements by using the words 'anticipates', 'believes', 'expects', 'intends' and similar expressions in such statements. Important factors that could cause actual results to differ materially from those contained in forward-looking statements, certain of which are beyond our control, include, among other things: the loss or expiration of, or limitations to, patents, marketing exclusivity or trademarks, or the risk of failure to obtain and enforce patent protection; the risk of substantial adverse litigation/government investigation claims and insufficient insurance coverage; effects of patent litigation in respect of IP rights; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the risk that strategic alliances and acquisitions, including licensing and collaborations, will be unsuccessful; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any delays in the manufacturing, distribution and sale of any of our products; the impact of any failure by third parties to supply materials or services; the risk of failure of outsourcing; the risks associated with manufacturing biologics; the risk of delay to new product launches; the difficulties of obtaining and maintaining regulatory approvals for products; the risk of failure to adhere to applicable laws, rules and regulations; the risk of failure to adhere to applicable laws, rules and regulations relating to anti-competitive behaviour; the risk that new products do not perform as we expect; failure to achieve strategic priorities or to meet targets or expectations; the risk of an adverse impact of a sustained economic downturn; political and socio-economic conditions; the risk of environmental liabilities; the risk of occupational health and safety liabilities; the risk associated with pensions liabilities; the risk of misuse of social medial platforms and new technology; the risks associated with developing our business in emerging markets; the risk of illegal trade in our products; the risks from pressures resulting from generic competition; the risk of failure to successfully implement planned cost reduction measures through productivity initiatives and restructuring programmes; economic, regulatory and political pressures to limit or reduce the cost of our products; the risk that regulatory approval processes for biosimilars could have an adverse effect on future commercial prospects; the impact of failing to attract and retain key personnel and to successfully engage with our employees; the impact of increasing implementation and enforcement of more stringent anti-bribery and anti-corruption legislation; and the risk of failure of information technology and cybercrime. Nothing in this presentation / webcast should be construed as a profit forecast.

# 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

| | | |
|---|---|---|
| **Overview** | Pascal Soriot |  |
| **Opportunity** | Luke Miels |  |
| **Clinical** | Sean Bohen |  |
| **Terms** | Marc Dunoyer |  |
| **Summary** | Pascal Soriot |  |

# 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 hyperkaleamia in the US**

**Global potential peak-year sales >$1bn**

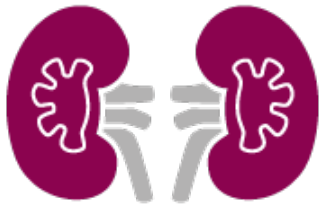
**Transaction supports Return to Growth strategy**

- 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**

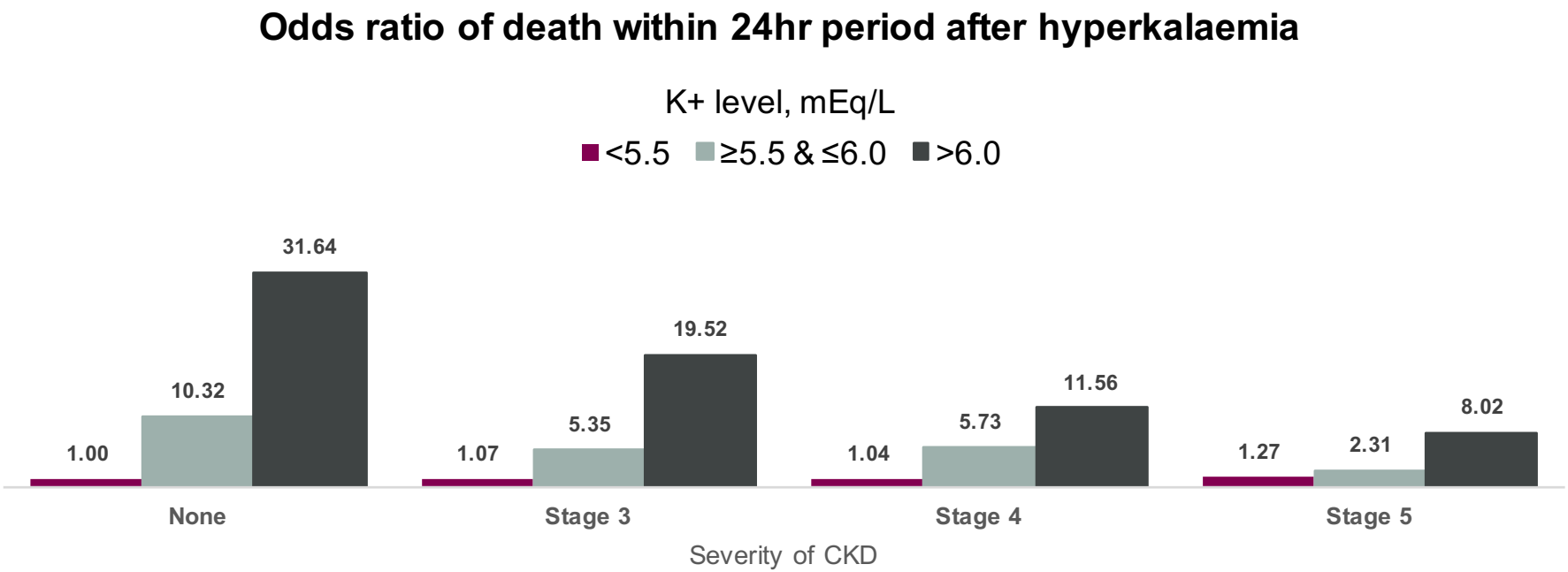
| Cardiovascular | Metabolism | CKD |
| --- | --- | --- |
|  |  |  |

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

# About ZS Pharma

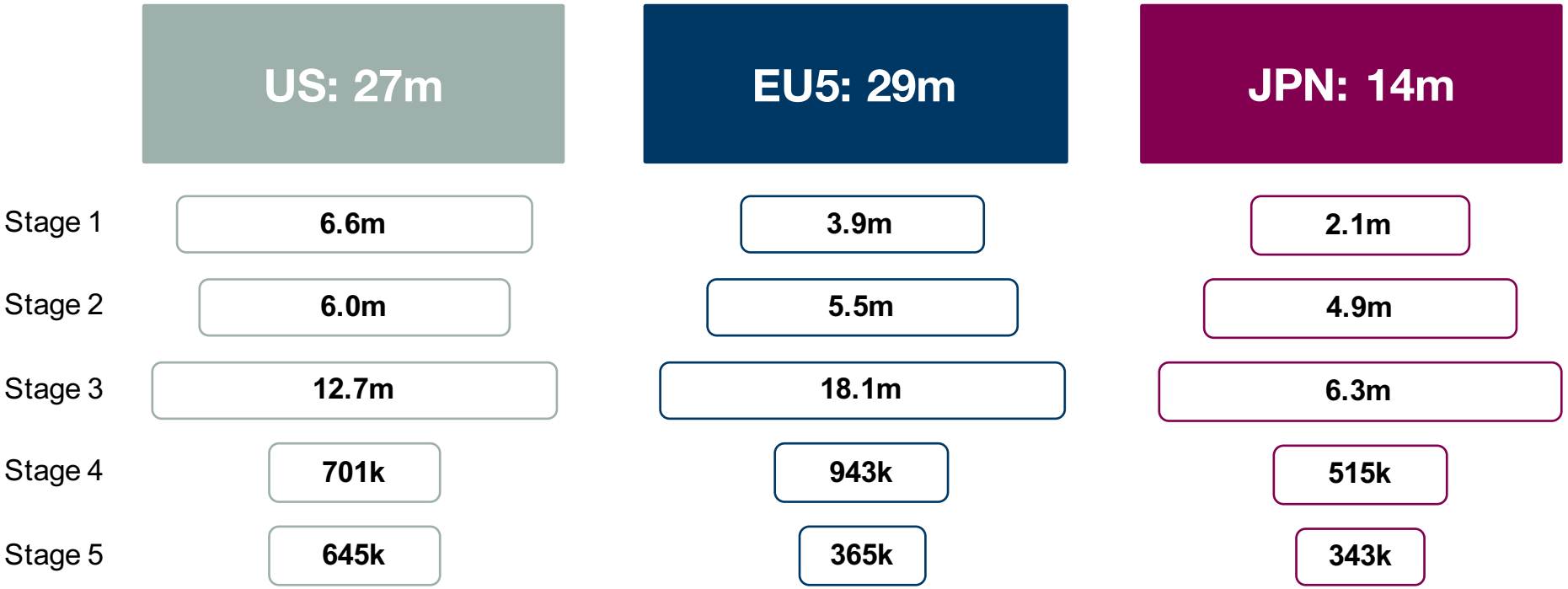
- Publicly traded (NASDAQ: ZSPH)
- Founded in 2008; headquartered in San Mateo, California
- Development manufacturing site in Coppell, Texas
- ~200 employees
- Strong expertise, know-how and capabilities in CKD
- Net cash position

# Hyperkalaemia is a leading cause of mortality in CKD




**Source:** *Arch Intern Med.* 22 June 2009; 169(12): 1156-1162.doi:10.1001/archinternmed.2009.132.

# CKD prevalence in key markets




**Source:** Decision Resources Group, Chronic Kidney Disease Patient Base, May 2015

REVIEWS

## 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]**

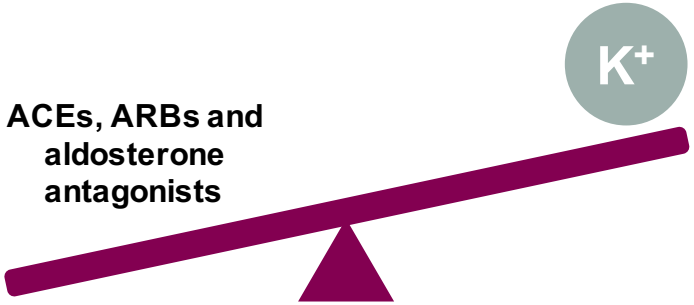
**20 – 50%**

**CKD**

**Up to 20%**

**CHF**

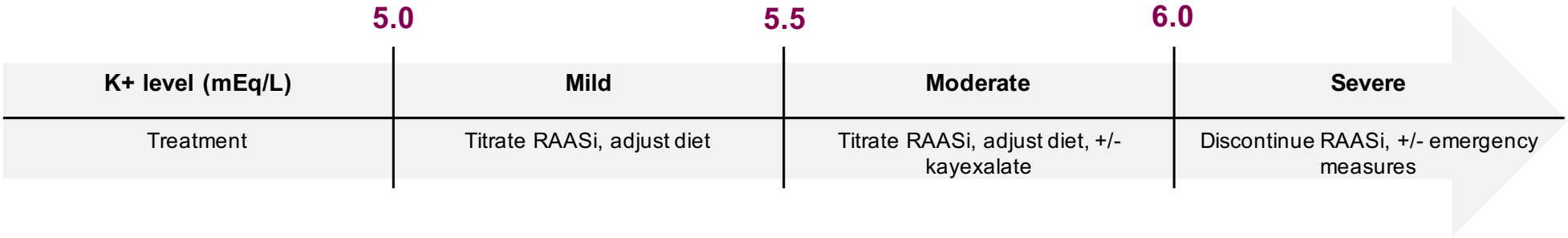
**… and on lifesaving RAASi therapies**




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

**Source:** Einhorn LM, Zhan M, Hsu VD, et al. The frequency of hyperkalemia and its significance in CKD. Arch Intern Med. 2009;169(12):1156-1162. doi:10.1001/archinternmed.2009.132.

# Limited alternative treatment options




**Current treatment options**

**Phase I, II, III:** 0

**Submitted:** ZS-9

**Approved:** patiromer

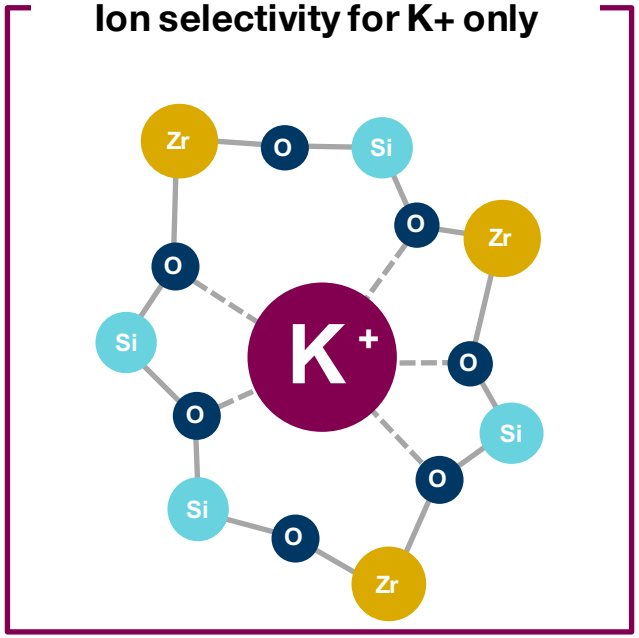
**Marketed:** kayexalate

**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

**Crystal structure**
**Ion selectivity for K+ only**

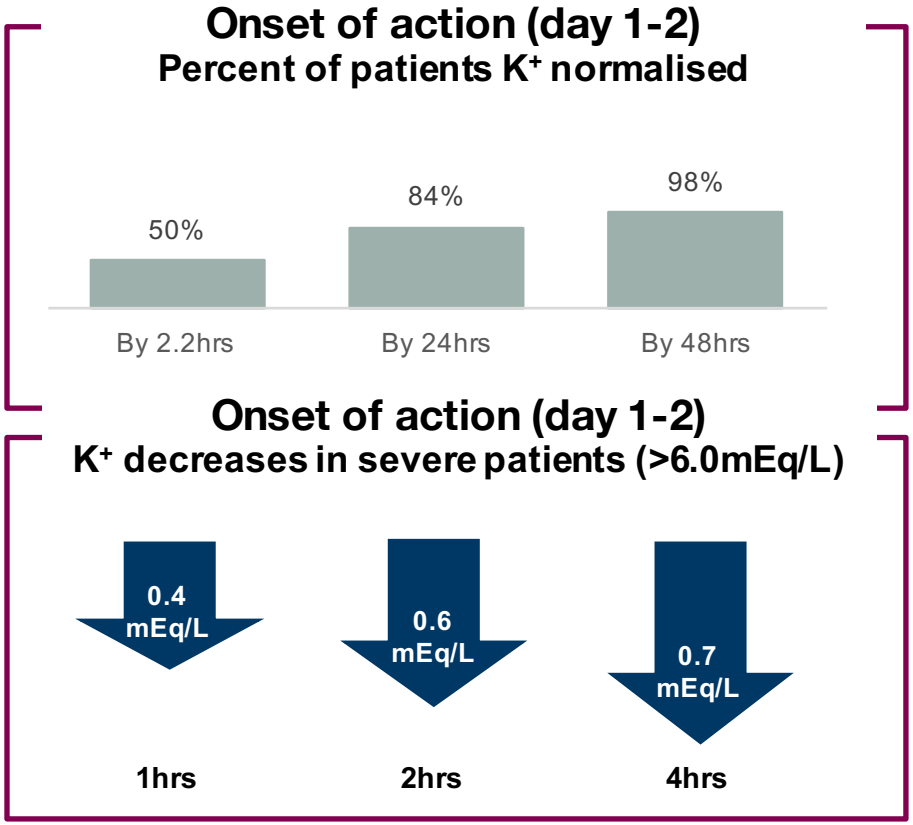


# ZS-9: ~1,700 patients in clinical development programme

| Trial | Published | Trial type | # Patients | Duration | Endpoint |
|---|---|---|---|---|---|
| **ZS002 (Completed)** | kidney INTERNATIONAL | Phase II Double-blind RCT | N=90 Serum K 5.0–6.0 mEq/L | 48 hours | Δ serum K+ level (3 doses) ✓ |
| **ZS003 (Completed)** | The NEW ENGLAND JOURNAL of MEDICINE | Phase III Double-blind RCT | N=753 Serum K 5.0–6.5 mEq/L | 14 days | Δ serum K+ level (4 doses) ✓ |
| **ZS004e (Completed/ extension ongoing)** | JAMA® The Journal of the American Medical Association | Phase III Double-blind RCT | N=258 Serum K >5.0 mEq/L | 1 month + 11 month extension | Maintenance of serum K+ (28 days) ✓ |
| **ZS005 (Ongoing)** | | Open-label safety trial | N=750 Serum K >5.0 mEq/L | 12 months | Safety & tolerability of long-term dose (initiated Q2 2014) |

# ZS-9: Efficacy summary

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




**Source:** Aggregated clinical trial data from company due diligence. Data on file.

# 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 subsidary
- 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-accretive from 2018; marginally dilutive in 2016 & 2017

# Questions