

9-MONTH GROUP COMMUNICATION 2016

# EpiScience for Life

4SC 

## ABOUT THIS REPORT

This 9-Month Group Communication 2016 should be read in conjunction with 4SC's Annual Report for the 2015 financial year, the 3-Month Group Communication 2016 and the 6-Month Consolidated Financial Report 2016.

The 9-Month Group Communication 2016 contains certain forward-looking statements that are subject to risks and uncertainties that are described, with no claim to be exhaustive, in the section entitled "Report on opportunities and risks" in the Annual Report 2015 and also in the "Opportunities and risks" section of this 9-Month Group Communication 2016. In many cases, these risks and uncertainties are outside of 4SC's control and may cause actual results to differ materially from those contemplated in these forward-looking statements. 4SC expressly does not assume any obligation for updating or revising forward-looking statements to reflect any changes in the parties' expectations or in events, conditions or circumstances on which such statements are based.

Since the end of November 2015, companies listed on the Prime Standard segment of the Frankfurt Stock Exchange are no longer obliged to prepare full-length quarterly financial reports. Instead, the regulatory requirements for 3- and 9-month reporting have been limited to quarterly communication with a much less extensive scope. 4SC has elected to take advantage of this new flexibility. Compared with the previous year, 4SC focused its interim reporting more on presenting key developments that are relevant for evaluating the Company.

## ABOUT 4SC

4SC ([www.4sc.com](http://www.4sc.com)) is a biotech company dedicated to the research and development of small-molecule drugs focused on epigenetic mechanisms of action for the treatment of cancers with high unmet medical needs. These drugs are intended to provide innovative treatment options for cancer patients that are more tolerable and efficacious than existing therapies, provide a better quality of life and offer increased life expectancy. The Company's pipeline comprises promising products that are in various stages of clinical development. 4SC's aim is to generate future growth and enhance its enterprise value by entering into partnerships with pharmaceutical and biotech companies. Founded in

1997, 4SC had 47 employees as of 30 September 2016. 4SC has been listed on the Prime Standard of the Frankfurt Stock Exchange since December 2005.

## KEY EVENTS IN Q3 2016 AND BEYOND

The events mentioned here were each made public via an ad hoc or press release. Details about these events can be found in the relevant releases (available at [www.4sc.com](http://www.4sc.com)) and in the business review information in this 9-Month Group Communication 2016.

### 20 July

4SC forms international Scientific Panel; renowned experts in the fields of epigenetics and oncology will provide 4SC with guidance on research and its clinical value

### 21 September

Dr Jason Loveridge, internationally experienced life sciences executive and investment professional, appointed new CEO of 4SC effective immediately

### 28 September

4SC sells immunology portfolio to Immunic and continues to focus its epigenetics strategy on key oncology assets

### 29 September

4SC hosts 11th Scientific Symposium on "Epigenetics: Reprogramming cancer – overcoming drug resistance", with internationally renowned experts presenting and discussing recent developments in the field of epigenetic cancer therapy

### 5 October

Following the previously announced headline results from Yakult Honsha's Phase II trial of 4SC's resminostat in combination with sorafenib as first-line therapy in advanced liver cancer, detailed subgroup analysis suggests a significant survival benefit in patients with higher than median platelet count at study entry; based on these results, 4SC and Yakult Honsha are currently discussing plans for continued clinical development of resminostat in this indication

## 21 October

Dr Daniel Vitt will step down as Chief Development Officer and Chief Scientific Officer (CDO/CSO) at the end of 2016; Dr Frank Hermann, who recently joined from Bristol-Myers Squibb, is promoted to CDO, and Dr Roland Baumgartner, who has been with 4SC for 14 years in Translational Pharmacology, is promoted to CSO

## DEVELOPMENT OF CASH FUNDS IN Q3 2016

As of 30 September 2016, 4SC holds cash balance/funds of €12,266 thousand (30 June 2016: €13,798 thousand). The decrease was attributable to monthly use of cash from operations amounting to €1,230 thousand on average in Q3 2016 after €1,243 thousand in H1 2016. These figures are similar to the figure forecast for 2016 as a whole of €1,200 thousand. The deviations from forecast largely relate to slightly higher costs for preparing and running the planned Phase II clinical trial of resminostat in cutaneous T-cell lymphoma (CTCL) than anticipated.

## FINANCIAL FORECAST

The Management Board of 4SC confirms its current financial forecast for the full year 2016 and further estimates that the funds earmarked for the Company's financing will probably be sufficient until early 2018 and will continue to fund the planned trial of resminostat in CTCL.

## BUSINESS REVIEW Q3 2016 AND OUTLOOK

In Q3 2016, 4SC further strengthened focus on the clinical development of its two epigenetic cancer compounds resminostat and 4SC-202.

## DEVELOPMENT SEGMENT

As of 30 September 2016, the Development segment comprised the oncology drug candidates resminostat, 4SC-202 and 4SC-205, with the two epigenetic drug candidates resminostat and 4SC-202 in key focus of the Company's development efforts. The autoimmune candidate vidofludimus was sold on 28 September 2016 and is therefore no longer included in the Development segment.

## ONCOLOGY

### RESMINOSTAT

Resminostat is an orally administered epigenetic anti-cancer compound. As an inhibitor of HDAC (histone deacetylase) that targets class I, IIB, and IV HDACs, resminostat can reactivate e.g. silenced genes in cancer cells or conversely downregulate abnormally expressed genes. In addition to its direct effects, resminostat enhances the body's own immune response to cancer.

Resminostat is in development both as monotherapy and in combination with other drugs. The compound has been shown to be well tolerated in Phase I studies, and its use in the treatment of CTCL, Hodgkin's lymphoma and liver, lung, colon, pancreatic and biliary tract cancers is being investigated in further clinical studies. Initial positive efficacy results for resminostat monotherapy have already been observed in patients with Hodgkin's lymphoma and in combination with the standard medication sorafenib in selected patients with advanced liver cancer (HCC).

4SC is finalizing preparations for the RESMAIN randomized, placebo-controlled Phase II clinical trial of resminostat in CTCL. This trial will be conducted in Europe to examine resminostat as maintenance therapy to delay or prevent the progression of disease in patients with advanced CTCL who have benefitted from a prior systemic therapy. 4SC finalized the study design in Q1 2016, following scientific advice from the European Medicines Agency (EMA). The study will enroll 150 patients in 10 countries at 50 trial centers. 4SC expects top line results to be available in 2019. If the results are positive, the Company intends to immediately submit this data to the relevant regulatory agencies for market approval.

Yakult Honsha Co., Ltd. (Yakult Honsha), 4SC's Japanese development partner, continues to make solid progress with the clinical development of resminostat. In May 2016, 4SC announced headline results from Yakult Honsha's Phase II trial of resminostat in combination with the standard-of-care drug sorafenib as first-line therapy in Asian patients in Japan and South Korea with advanced liver cancer (HCC). While the primary endpoint

of statistically significant prolonged time to disease progression (TTP) compared to sorafenib monotherapy was not reached in the all-comer patient population, 4SC announced on 5 October that subgroup analysis indicated a significant survival benefit in patients with higher than median platelet count at study entry. Based on these results, 4SC and Yakult Honsha are currently discussing their plans for continued clinical development of resminostat. The results of the finalized HCC study will be published by Yakult Honsha and the investigators at an upcoming scientific conference.

Menarini AP, 4SC's second development partner for resminostat, is also actively reviewing the clinical development options for resminostat in the Asia-Pacific region, excluding Japan.

#### 4SC-202

4SC-202 is an orally administered epigenetic anti-cancer compound with a unique mechanism of action. 4SC-202 is an LSD1 (lysine-specific demethylase) and HDAC1, 2, 3 (histone deacetylase) inhibitor that can reactivate deactivated genes or conversely downregulate abnormally expressed genes e.g. in cancer cells.

4SC-202 also inhibits cells utilizing the Hedgehog and WNT signaling pathways, which play an important role in the development and metastasis of cancer. 4SC-202 is thought to be the only blocker of the SMO protein-independent Hedgehog pathway in clinical development and could also provide treatment options for those cancers for which other Hedgehog inhibitors to date have been ineffective or have shown resistance. In addition to the direct effects, 4SC-202 can also enhance the body's own immune response to cancer.

In a Phase I trial evaluating the compound in patients with advanced hematological malignancies and lymphomas, 4SC-202 proved to be well tolerated. Encouraging signs of efficacy were also observed - the disease regressed completely in one patient and partially in another.

Preclinical results presented in H1 2016 demonstrate that 4SC-202 is an effective combination partner for checkpoint inhibitors when treating cancer. Tumors exploit immune system "checkpoints" to switch off an immune response. This promising immunological data presents an opportunity for the clinical development of 4SC-202 in patients with hematological, lung or skin cancer in mono- and combination therapy. 4SC is engaged in discussions with potential financing and industry partners to secure the further development of 4SC-202 in a number of individual Phase II clinical programs.

#### 4SC-205

4SC-205 is an orally administered anti-cancer compound. 4SC-205 inhibits the kinesin spindle protein Eg5 (KIF11) which plays a key role in cancer cell division and growth.

In a Phase I trial of the treatment of solid tumors, 4SC-205 proved to be well tolerated. As the only orally administered Eg5 inhibitor currently in clinical development, 4SC-205 can be taken daily at low doses. This ensures that the substance is steadily available in the body and can have a continuous effect. The dosing scheme also has a highly positive influence on the side effect profile. Serious adverse reactions of the peripheral nervous system - known from drugs with a similar mechanism of action - were not observed with the use of 4SC-205.

In line with the May 2016 licensing and development agreement between 4SC and Guangzhou LingSheng Pharma Tech Co., Ltd (Link Health) for the further development of 4SC-205 in Greater China (China, Hong Kong, Taiwan and Macao), 4SC can use Link Health's findings to pursue the further development of 4SC-205 in other parts of the world as well, potentially also through additional independent partnerships.

## **AUTOIMMUNE DISEASES**

### **VIDOFLUDIMUS**

In line with 4SC's strategy to focus its activities on key epigenetic oncology assets, vidofludimus was sold to Immunic AG (Immunic) on 28 September 2016 for a one-time upfront and milestone payments as well as royalties.

## **DISCOVERY & COLLABORATIVE BUSINESS SEGMENT**

Until April 2016, the Discovery & Collaborative Business segment comprised the activities involved in the discovery, early-stage research and subsequent commercialization of drug compounds by 4SC Discovery GmbH (4SC Discovery). In addition to maintaining scientific collaborations with academic institutions, 4SC Discovery also cooperated with BioNTech AG (BioNTech) and had a technology and sales partnership with CRELUX GmbH, among others.

In April, 4SC sold all key operating assets of 4SC Discovery to a subsidiary of BioNTech, and all 22 former 4SC Discovery employees transferred to BioNTech as of the beginning of May. 4SC can continue to use the underlying intellectual property for its own purposes.

## **SIGNIFICANT EVENTS AT GROUP LEVEL**

On 20 July 2016, 4SC announced the formation of an international Scientific Expert Panel (iSEP). The panel is comprised of renowned experts in the fields of epigenetics and oncology, who will support 4SC in further expanding its leadership position in the development of epigenetic cancer drugs. The iSEP's inaugural members are Prof Dr Thomas Jenuwein, Dr Charles B. Epstein and Prof Dr med. Wolff Schmiegel.

On 21 September, the Supervisory Board of 4SC appointed Dr Jason Loveridge as the new CEO of 4SC with immediate effect. Jason Loveridge has a scientific background in Biochemistry and Microbiology as well as more than 20 years international experience across Europe, Asia and the US in senior management positions in life sciences companies and as an investment

professional dealing with both privately held and publicly traded companies.

On 29 September 2016, 4SC hosted its 11th Scientific Symposium, themed "Epigenetics: Reprogramming cancer – overcoming drug resistance", with internationally renowned experts presenting and discussing recent developments in the field of epigenetic cancer therapy.

## **EVENTS AFTER Q3 2016**

4SC announced headline results from Yakult Honsha's Phase II trial of resminostat in combination with the standard-of-care drug sorafenib as first-line therapy in Asian patients in Japan and South Korea with HCC in May 2016. While the primary endpoint of statistically significant prolonged time to disease progression (TTP) compared to sorafenib monotherapy was not reached in the all-comer patient population, 4SC announced on 5 October that subgroup analysis indicated a significant survival benefit in patients with higher than median platelet count at study entry. Based on these results, 4SC and Yakult Honsha are currently discussing their plans for continued clinical development of resminostat in this indication. The results of the finalized HCC study will be published by Yakult Honsha and the investigators at an upcoming scientific conference.

On 21 October, 4SC announced that Dr Daniel Vitt and the Supervisory Board of 4SC have agreed that Daniel Vitt will step down as Chief Development Officer and Chief Scientific Officer (CDO/CSO) as well as from the Management Board of 4SC as of 31 December 2016. Dr Frank Hermann, who recently joined from Bristol-Myers Squibb, is promoted to CDO, and Dr Roland Baumgartner, who has been with 4SC for 14 years in Translational Pharmacology, is promoted to CSO.

## **OPPORTUNITIES AND RISKS**

Please see pages 57 to 69 of the Annual Report 2015 for a detailed description of the risks and opportunities arising from the Company's business activities as well as its IT-based risk management and controlling system. In

the 6-Month Consolidated Financial Report 2016, 4SC stated that the topline results published on 27 May 2016 of the Phase II trial conducted by Yakult Honsha of resminostat in combination with sorafenib as a first-line therapy for liver cancer patients and Yakult Honsha's related decision not to conduct a pivotal study in this indication in all-comer patients have increased both the product development risks and the required financing compared to the information provided in the Annual Report 2015. With the insights provided by the subgroup analysis announced on 5 October, suggesting survival benefit in patients with higher than median platelet count at study entry, 4SC believes that these risks have subsequently decreased. The Company's risks and opportunities have otherwise remained virtually unchanged. The occurrence of any one of the risks described in the annual report – alone or in conjunction with each other – could have a negative impact on the results of operations, financial position and net assets of 4SC.

## FINANCIAL CALENDAR

Annual Report 2016	29 March 2017
3-Month Group Communication 2017	27 April 2017
Annual General Meeting 2017	6 July 2017
6-Month Consolidated Financial Report 2017	10 August 2017
9-Month Group Communication 2017	26 October 2017

## PUBLISHING INFORMATION

### EDITOR

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### 4SC ON THE INTERNET

More information about 4SC, its products and R&D programs, is available on the Company's website, [www.4sc.com](http://www.4sc.com), as well as the following information:

- this interim communication
- previous interim reports
- annual reports
- audio recordings of conference calls
- presentations
- general investor information

## CORPORATE COMMUNICATIONS & INVESTOR RELATIONS

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