

Combined FOXFIRE Analysis Shows No Improvement in Overall Survival in mCRC

- The primary endpoint of Overall Survival (OS) showed no statistically significant difference between SIR-Spheres plus chemotherapy versus chemotherapy alone (Hazard Ratio (HR)= 1.04; 95% Confidence Interval (CI) 0.90-1.19, p=0.609) in first-line mCRC patients
- No statistically significant difference in Overall Progression-Free Survival (PFS) between SIR-Spheres plus chemotherapy versus chemotherapy alone (HR=0.90, 95% CI 0.79-1.02, p=0.108)
- There was also no statistically significant difference in OS in either the Liver-Only disease and Liver-Dominant disease sub-groups
- Exploratory analyses of SIRFLOX/FOXFIRE Global data showed a statistically significant 4.9 month improvement in median OS in patients with a right-sided¹ primary colon cancer favouring the SIR-Spheres plus chemotherapy arm (HR=0.64, 95% CI 0.46-0.89, p=0.007)

Sirtex will host an **Investor Conference Call** to discuss the SIRveNIB and SIRFLOX/FOXFIRE/FOXFIRE Global clinical study results, including a Q&A session at **1:00 pm AEST today**.

Conference ID: 1973 1589

Toll Free Dial-in Details: Australia Toll Free: 1800 123 296, Australia Local Dial: +61 2 8038 5221, USA: 1855 293 1544, United Kingdom 0808 234 0757 (other countries – see end of release)

Sydney, Australia; 18th May 2017 – Sirtex Medical Limited (ASX:SRX) today announces the results of the combined SIRFLOX/FOXFIRE/FOXFIRE Global studies comparing SIR-Spheres[®] Y-90 resin microspheres plus standard of care systemic chemotherapy versus systemic chemotherapy alone in non-resectable, first-line metastatic colorectal cancer (mCRC) patients. The abstract was published on-line ahead of the upcoming American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

Mr Nigel Lange, Interim CEO of Sirtex Medical said “We are disappointed that the combined analyses did not meet the primary endpoint of an Overall Survival benefit in these first-line patients and that no statistically significant survival benefit was observed in the pre-specified sub-groups, including those patients with metastatic disease confined to their liver. The study finding of a statistically significant 36% reduction in the risk of death in patients with right-sided colon cancers who received SIR-Spheres plus chemotherapy requires further investigation as the clinical meaningfulness has yet to be determined.

Mr Lange continued “Commercially, management expect this to have minimal impact on our current business as the vast majority of the mCRC patients we currently treat have failed all of the standard chemotherapy treatments. In our existing markets this represents an annual opportunity of 42,000 patients. The use of SIR-Spheres within the salvage setting is supported by extensive scientific evidence and is recommended in treatment guidelines across the globe for mCRC. Additionally, there will be no impact to any of our regulatory approvals globally from this study outcome.”

Professor Ricky Sharma, the Principal Investigator of the FOXFIRE study and Chair of Radiation Oncology at University College London, will present the oral abstract at ASCO. The study authors concluded in the abstract “*Despite higher response rates and improved liver-specific PFS, the addition of SIRT to first-line oxaliplatin-fluorouracil chemotherapy for patients with liver-only and liver-dominant mCRC did not improve OS or PFS.*”

The combined SIRFLOX/FOXFIRE/FOXFIRE Global study was the largest ever interventional oncology study with a liver-directed therapy, namely SIR-Spheres microspheres, to examine OS in the first-line mCRC setting with standard of care systemic chemotherapy with or without biologic therapy. A total of 1,103 patients were enrolled across all three studies. The oral abstract will be presented at ASCO on the 5th of June.

As indicated, an initial exploratory analysis undertaken of the combined SIRFLOX and FOXFIRE Global studies revealed a 4.9 month improvement in median OS in patients who had their primary colon cancer located on the right-side of the colon and who received SIR-Spheres plus chemotherapy versus chemotherapy alone and a 36% decreased risk of death (HR=0.64, p=0.007). Approximately 24% of patients enrolled in these two studies had a right-sided primary tumour. There was no benefit conferred in patients who had their primary tumour on the left-side² of the colon. Information on the location of the primary tumour in the colon was collected prospectively, but patients were not stratified on this basis under the three original study protocols.

The data on the impact of primary tumour location on overall survival will be presented at the 19th European Society for Medical Oncology (ESMO) World Congress on Gastrointestinal Cancer (WCGIC) in Barcelona, Spain from 28th June to 1st July.

This right-side primary tumour finding from the study requires further investigation. There is now increased evidence that supports primary tumour location (left-side or right-side) as being an important prognostic factor in both early and advanced colorectal cancer. Tumours that arise in the right-side of the colon are clinically and biologically distinct from tumours on the left-side of the colon. The incidence of right-sided primary colon cancers averages 38% in mCRC patients, based on clinical studies and population-based analysis.³ Colon cancer patients who present with a right-sided primary tumour in their colon are clinically more difficult to treat, being less responsive to standard of care chemotherapies and biologic agents. A meta-analysis of 66 studies representing 1.4 million patients showed an 18% reduced risk of death from a left-side primary tumour versus a right-side primary tumour regardless of the patient's disease stage.³ For mCRC patients, there was a 27% reduced risk of death in those patients with a left-sided primary tumours compared to right-sided primaries. Other analyses also support this observation of a worse prognosis with lower overall survival from right-sided primary tumours.^{4,5}

Acknowledging the increased evidence of ‘sidedness’ in colorectal cancer patient management, the current National Comprehensive Cancer Network (NCCN) guidelines for first-line treatment of mCRC recently included treatment recommendations based on the location of the primary tumour.⁶

The preliminary nature of this study finding means that Sirtex is unable to confirm whether such data is clinically meaningful and likely to result in any change to clinical practice in first-line mCRC patients with a right-sided primary colon cancer. Sirtex anticipates that following presentation of further data at WCGIC and peer review, the Company will be in a position to assess the commercial implications, if any, from presentation of the data and consultation with experts in the field.

Summary of Abstract⁷ Results:

- Median age was 63 years (range 23-89); median follow-up 43.3 months and 844 deaths.
- There was no difference in OS (HR=1.04; 95% CI 0.90-1.19, p=0.609) or PFS (HR=0.90, 95% CI 0.79-1.02, p=0.108) between the two arms of the study.
- Objective response rate (p=0.001) and liver-specific progression (HR=0.51, 95% CI 0.43-0.62, p<0.001) were significantly more favourable in SIR-Spheres plus chemotherapy arm.

- Patients in SIR-Spheres plus chemotherapy arm had higher risk of non-liver progression as first event (HR=1.98, 95% CI 1.53-2.58, p<0.001).
- Grade 3-5 adverse events were more common in SIR-Spheres plus chemotherapy arm (74.0%) than chemotherapy alone (66.5%), p=0.009.
- In health status questionnaires, EQ-5D utility scores were not significantly different between Arms at 6, 12 or 24 months.

The oral abstract released by ASCO can be viewed here:

http://abstracts.asco.org/199/AbstView_199_184921.html

Conference Call Details:

Time: 1:00 pm AEST today.

Participants are encouraged to register at least 5-10 minutes prior to the commencement of the call, using the details provided, below.

Conference ID: 1973 1589

Toll Free Dial-in Details:

Australia Toll Free: 1800 123 296

Australia Local Dial: +61 2 8038 5221

USA: 1855 293 1544

Hong Kong: 800 908 865

Singapore: 800 616 2288

United Kingdom: 0808 234 0757

New Zealand: 0800 452 782

Canada: 1855 5616 766

Japan: 0120 477 087

A recording of the call will be made available in the 'Investors' section of the Company website shortly after the conclusion of the call at: <http://www.sirtex.com/au/investors/>

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About SIRFLOX/FOXFIRE/FOXFIRE Global

The aim of the SIRFLOX/FOXFIRE/FOXFIRE Global studies is to prospectively combine clinical data from the three similarly designed individual trials to allow adequate power to evaluate the impact of chemotherapy with Selective Internal Radiation Therapy (SIRT) using SIR-Spheres[®] Y-90 resin microspheres on overall survival in first-line metastatic colorectal cancer, in over 1,100 patients. Efficacy and safety estimates derived using individual participant data (IPD) from SIRFLOX, FOXFIRE, and FOXFIRE Global will be pooled using 2-stage prospective meta-analysis. Secondary outcome measures include progression-free survival (PFS), liver-specific PFS, health-related quality of life, response rate, resection rate, and adverse event profile. The potential treatment benefit in those patients who present with disease confined to the liver will be also be investigated.

About Colorectal Cancer

Colorectal cancer (CRC or bowel cancer) occurs when cancerous cells develop in the patient's colon or rectum. CRC is the third most common form of cancer worldwide, making up about 10% of all cancers. In 2012, an estimated 1.4 million new cases were diagnosed globally and 694,000 cancer deaths were attributed to CRC.⁸

About SIR-Spheres® Y-90 Resin Microspheres

SIR-Spheres Y-90 resin microspheres are a medical device used in interventional oncology and delivered via Selective Internal Radiation Therapy (SIRT), also known as radioembolisation, directly to liver tumours. SIR-Spheres Y-90 resin microspheres are approved for supply in key markets, such as the United States, European Union and Australia.

About Sirtex Medical

Sirtex Medical Limited (ASX:SRX) is an Australian-based global healthcare business working to improve outcomes in people with cancer. Our current lead product is a targeted radiation therapy for liver cancer. Over 73,000 doses have been supplied to treat patients with liver cancer at 1,060 medical centres in over 40 countries. For more information please visit www.sirtex.com.

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¹ The **right-side of the colon** is derived from the embryologic midgut, which encompasses the proximal two-thirds of the transverse colon, ascending colon and caecum

² The **left side of the colon** is derived from the embryologic hindgut, which includes the distal third of the transverse colon, splenic flexure, descending colon, sigmoid colon, and rectum

³ Petrelli et al., JAMA Oncology 3(2):211-219, 2017

⁴ Price et al., Cancer 121(6):830-835, 2015

⁵ Holsch et al., Eur J. Cancer 70:87-98

⁶ Clinical Practice Guidelines in Oncology (NCCN® Guidelines), Colon Cancer Version 2.2017 – March 13, 2017

https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf

⁷ Sharma RA et al. Overall survival analysis of the FOXFIRE prospective randomized studies of first-line selective internal radiotherapy (SIRT) in patients with liver metastases from colorectal cancer. *2017 ASCO Annual Meeting; J Clin Oncol* 2017; **35** (Suppl): Abs 3507.

⁸ World Cancer Report, 2014; Geneva, WHO: 2014; 1.1.