ASX/MEDIA RELEASE **24th April 2017**

SARAH Study Shows Statistically Significant Safety, Toxicity and Quality of Life Benefits for SIR-Spheres versus Sorafenib with No Difference in Survival

- **Per-Protocol (PP)[1] median Overall Survival (OS) in SIR-Spheres® Y-90 resin microspheres arm was identical to sorafenib (9.9 months, Hazard Ratio (HR)=0.99, p=0.92)**
- **Intention-To-Treat (ITT)[2] median OS in SIR-Spheres microspheres arm of 8.0 months versus 9.9 months in the sorafenib arm was not significantly different (HR=1.15, p=0.18)**
- **Statistically significant safety and toxicity benefits and significantly improved Quality of Life (QoL) favouring SIR-Spheres microspheres**
- **Sirtex will immediately commence sales and marketing activities on the SARAH result across EMEA and APAC**
- **Additional regulatory filings in the USA planned during 2H CY17**

Sirtex will host an **Investor Conference Call and Webcast** with presentation slides to discuss the SARAH clinical study results, including a Q&A session at **9:00 am AEST today**.
Conference ID: 4892 808
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)
Webcast Link: http://webcast.openbriefing.com/3666

Sydney, Australia; 24th April 2017 – Sirtex Medical Limited (ASX:SRX) today announces the results of the 459 patient SARAH clinical study comparing SIR-Spheres® Y-90 resin microspheres versus the current standard-of-care systemic therapy sorafenib (Nexavar®, Bayer Healthcare Pharmaceuticals) in patients with non-resectable advanced hepatocellular carcinoma (HCC), the most common type of primary liver cancer. While the study did not meet the primary endpoint of OS superiority versus sorafenib in the ITT analysis, it showed both treatments resulted in a similar OS in patients with beneficial safety, toxicity and Quality of Life (QoL) favouring SIR-Spheres microspheres.

Mr Nigel Lange, Interim CEO of Sirtex Medical said "Although SARAH study did not meet the primary endpoint of an OS benefit versus sorafenib, it is important to note that 27% of patients randomised to SIR-Spheres microspheres in the ITT analysis didn't receive our treatment. The median time from randomisation to treatment was unusually long at 29 days relative to real world clinical experience, and a high proportion of difficult to treat patients with vascular invasion (PVT) of their disease were enrolled. Pleasingly, SIR-Spheres showed identical median OS to sorafenib in the PP analysis of 9.9 months and conferred significant safety, toxicity and tolerability benefits to patients versus sorafenib across a range of parameters and significantly better Quality of Life. We remain very excited by the prospects this result holds for our sales and marketing initiatives as we seek to educate clinicians and government/private payers on these benefits coupled with additional regulatory filings in the US planned for the second half of calendar year 2017."

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The SARAH study is the first ever large randomised controlled trial with Level I clinical evidence to demonstrate that a liver-directed therapy, namely SIR-Spheres Y-90 resin microspheres, offers patients a similar overall survival benefit to the current standard of care chemotherapy agent sorafenib with significantly less side-effects and improvements in the quality of the patient's life.

Professor Valérie Vilgrain MD, PhD, Principal Investigator of the SARAH study, Head of Department of Radiology, Beaujon Hospital, AP-HP and Professor at the Université Paris Diderot, Sorbonne Paris Cité, France, said that "In terms of what matters for patients, the findings from this first large head-to-head comparison of liver-directed Selective Internal Radiation Therapy (SIRT) and systemic chemotherapy with sorafenib also show clearly that liver-directed procedures with SIR-Spheres result in a significantly better tolerance of treatment and quality of life. I believe this consideration should be a critical factor in selecting first-line treatment for this patient population in the future."

Professor Bruno Sangro MD, PhD Director of the Liver Unit at Clinica Universitaria de Navarra, Professor of Medicine at the University of Navarra School of Medicine, and senior researcher in the National Biomedical Research Network Center for Liver and Digestive Diseases commented "SARAH provides confirmation in a multi-centre study setting that SIRT is safe and reliable, even for the most advanced patients. SIR-Spheres may provide patients with an alternative option to an effective systemic therapy that is often not well tolerated. The results will reassure current users and get the attention of those non-users concerned about the potential safety of SIRT in cirrhotic patients. The SARAH study results will increase the presence of this technology in multi-disciplinary team discussions."

Professor Jens Ricke MD, PhD, Principal Investigator of the SORAMIC study, University of Munich, Germany said "The favourable toxicity profile seen in the SARAH study for SIR-Spheres resin microspheres will have a compelling impact on clinical practice. Toxicity makes a difference when speaking with patients, as they are concerned about the impact of side effects such as fatigue, hand-foot syndrome or diarrhoea. For inoperable HCC patients in the out-patient setting, side effects of any therapy are very important. I believe it is a very compelling argument when discussing options with patients and families to start with Y90 which has a highly favourable toxicity profile – and add the systemic option as soon as needed. In patients with liver-limited inoperable HCC, the question now is, why not start treatment with SIR-Spheres / this technology, and reserve sorafenib for progressive disease – until we know from SORAMIC if a direct combination is even more favourable?"

The study was presented as an oral abstract at the 2017 European Association for the Study of the Liver, International Liver Congress™ 2017 in Amsterdam, the Netherlands[3].

A summary of the key findings of the SARAH abstract and oral presentation were as follows:

Efficacy Measures

- Per-Protocol (PP) median Overall Survival (OS) in the SIR-Spheres microspheres arm was identical to sorafenib (9.9 months, Hazard Ratio (HR)=0.99; 95% Confidence Interval (CI): 0.79-1.24; p=0.92).

- Intention-To-Treat (ITT) median OS in the SIR-Spheres microspheres arm of 8.0 months versus (*vs*.) 9.9 months in the sorafenib arm was not significantly different (HR=1.15; 95% CI: 0.94-1.41; p=0.18).

- PP median overall Progression-Free Survival (PFS) in the SIR-Spheres microspheres arm of 4.3 months vs. 3.7 months in the sorafenib arm was not significantly different (HR=0.97; 95% CI: 0.79-1.20; p=0.77).

- ITT median overall PFS in the SIR-Spheres microspheres arm of 4.1 months vs. 3.7 months in the sorafenib arm was not significantly different (HR=1.03; 95% CI: 0.85-1.25; p=0.76).

- Objective response rate (complete response + partial response) in the SIR-Spheres microspheres arm of 19% vs. 11.6% in the sorafenib arm was statistically significant (p=0.042).

- Statistically significant reduction in risk of cancer progressing in the liver in the SIR-Spheres microspheres arm vs. sorafenib (p=0.014).

- OS was similar between treatments in the following sub-groups:
    - Demographic characteristics: age, sex
    - Severity of the disease: ECOG score, cirrhosis, BCLC classification, Child-Pugh score, TACE failure
    - Tumour characteristics
    - Laboratory exams: alpha-fetoprotein, albumin, alkaline phosphatase and bilirubin

Safety, Toxicity and Quality of Life measures

- Significantly fewer patients treated with SIR-Spheres Y-90 resin microspheres had any treatment-related side effects at all (76.5% *vs*. 94.0% for sorafenib; p<0.001), and these were also less severe (grade ≥3; 40.7% *vs*. 63.0%, respectively; p<0.001). Patients treated with SIR-Spheres microspheres who reported treatment-related side effects experienced a median of only 5 such events over the course of the SARAH study, compared to a median of 10 events in those who received sorafenib (p<0.001).

- General treatment related symptoms such as fatigue (42% *vs*. 65%; p<0.001), abdominal pain (20% *vs*. 29%; p=0.032), nausea or vomiting (12% *vs*. 23%; p=0.001) and infection (4% *vs*. 11%; p=0.007) were also significantly less frequently reported and less severe for patients receiving SIR-Spheres Y-90 resin microspheres, compared to sorafenib.

- Fewer patients receiving SIR-Spheres microspheres experienced treatment related diarrhoea (13% *vs*. 68% for sorafenib; p<0.001), hand-foot skin reaction (0.4% *vs.* 21%; p<0.001), anorexia (13% *vs.* 32%; p<0.001), weight loss (6% *vs.* 21%; p<0.001) and alopecia (0% *vs.* 16%; p<0.001), as well as infections (4% *vs.* 11%; p=0.007), hypertension (3% *vs.* 13%; p<0.001) and non-gastrointestinal haemorrhage (3% *vs.* 10%; p=0.002).

- There were few potential SIRT-associated treatment-related complications and, importantly, no radioembolization-induced liver disease (radiation hepatitis) experienced. There were no significant increases for SIR-Spheres Y-90 resin microspheres in, for example, gastrointestinal (GI) ulceration (2% *vs.* 0.5% for sorafenib; p=0.37) including one case of radiation-induced GI ulcer, ascites (12% *vs.* 11%; p=0.57), hyperbilirubinaemia (12% *vs.* 13%; p=0.86) and only one case of radiation pneumonitis (0.4% *vs.* 0; p=0.46).

- Quality of Life (QoL) assessed in the European Organisation for Research and Treatment of Cancer [EORTC] QLQ-C30 questionnaire showed patients treated with SIR-Spheres maintained their health status over the duration of the SARAH study, whereas patients receiving sorafenib reported a significant and sustained decline in QoL (group effect: p=0.005; time effect: p<0.001; between group difference increase over time: p=0.045).

Other

- Further analyses from the study will include the cost-effectiveness of SIR-Spheres vs. sorafenib, dose-related efficacy in the SIR-Spheres group and prognostic factors.

- The study authors concluded “OS did not differ between sorafenib and SIRT. The liver-targeted treatment (SIRT) was more effective than the sorafenib systemic treatment in controlling tumour progression in the liver.”

The SARAH study abstract is available through the EASL website: https://ilc-congress.eu/ebooks/#abstract-book

Investors/analysts are also encouraged to read the associated investor presentation also released via the ASX today, which contains further details on the study outcomes as presented at the International Liver Congress™ 2017 with accompanying tables and graphical information.

Conclusions of the SARAH Study

Sirtex is pleased with the outcome of the SARAH study. The initial Key Opinion Leader (KOL) responses to the results have been positive. The study is supportive of SIR-Spheres as a new treatment option for clinicians to consider for their first-line HCC patients, given that in patients who received SIR-Spheres or sorafenib according to the SARAH protocol, median OS was identical.

Importantly, SIR-Spheres demonstrated significant safety, toxicity and tolerability benefits to patients versus sorafenib across a range of parameters. Moreover, patients treated with SIR-Spheres maintained their health status over the duration of the SARAH study, whereas patients receiving sorafenib reported a significant and sustained decline in Quality of Life.

Sirtex Strategies

Sirtex will immediately commence sales and marketing activities on the SARAH study results across EMEA, APAC, Latin America and Canada. In parallel, the company intends to engage in negotiations with European and country-specific treatment guideline panels for HCC. Furthermore, Sirtex plans to negotiate with various government/private payers on reimbursement for HCC, where limited or no reimbursement currently exists.

In the United States, SIR-Spheres is currently approved for inoperable metastatic colorectal cancer. Sirtex intends to submit for additional regulatory approvals in the US during 2H CY17.

Conference Call and Webcast Details:

Time: 9:00 am 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: 4892 808

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

Webcast Link: http://webcast.openbriefing.com/3666

A recording of the call and slide presentation 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 SARAH

SARAH (SorAfenib versus Radioembolisation in Advanced Hepatocellular carcinoma) is a Phase III multi-centre prospective randomised open-label study for patients in France with advanced HCC (Barcelona Clinic Liver Cancer stage C) with or without portal vein thrombosis and no extrahepatic spread, or whose disease has progressed or recurred after previous therapies; and who are ineligible for surgical resection, ablation or liver transplantation.

The primary goal of the SARAH study is to assess if radioembolisation with SIR-Spheres® Y-90 resin microspheres provides an increased survival benefit compared to sorafenib in patients with advanced HCC. The study is also comparing the quality of life of patients and other measures such as the tolerability of the treatments and healthcare costs associated with each intervention. For more information on the SARAH study, please visit: http://clinicaltrials.gov/ct2/show/NCT01482442

About Hepatocellular Carcinoma (HCC)

Hepatocellular Carcinoma (HCC) is the most common form of primary liver cancer – cancer that starts in the liver. It is the sixth most common cancer in the world and the second most common cause of cancer-related death[4].

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] **Per-Protocol (PP)** analysis is a comparison of treatment groups that includes only those patients who completed the treatment originally allocated. The PP analysis for SARAH included n=174 (SIR-Spheres arm) and n =206 (sorafenib arm).

[2] **Intention-To-Treat (ITT)** analysis is where all patients who were enrolled and randomly allocated to treatment are included in the analysis and are analysed in the groups to which they were randomised. The ITT analysis for SARAH included n=237 (SIR-Spheres arm) and n =222 (sorafenib arm).

[3] Vilgrain V *et al*. The International Liver Congress™ 2017 – 52nd annual meeting of the European Association for the Study of the Liver, *Journal of Hepatology* 2017; **66** (Suppl 1): Abs. GS-012.

[4] GLOBOCAN 2012. Estimated cancer mortality, incidence and prevalence worldwide. http://globocan.iarc.fr/Default.aspx