Ariad and STA Announce Approval of ICLUSIG™ (ponatinib) in Australia

Cambridge, MA, and Melbourne, Australia, November 24, 2014: ARIAD Pharmaceuticals, Inc. (NASDAQ: ARIA) and Specialised Therapeutics Australia Pty Ltd (STA), today announced the marketing approval of ICLUSIG™ (ponatinib) in Australia by the Therapeutic Goods Administration (TGA).

The Australian Product Information for ICLUSIG states that it is indicated for the treatment of adult patients with:

- Chronic phase, accelerated phase, or blast phase chronic myeloid leukaemia (CML) whose disease is resistant to, or who are intolerant of at least two prior tyrosine kinase inhibitors; or where there is a T315I mutation.
- Philadelphia-chromosome positive acute lymphoblastic leukaemia (Ph+ ALL) whose disease is resistant to, or who are intolerant of dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or where there is a T3151 mutation.

Therapy should be initiated and monitored by a haematologist with expertise in managing adult leukaemias.

“Up to thirty percent of patients with CML become resistant to current therapies, and patients with resistant disease eventually run low on treatment options,” said Professor Timothy Hughes, Consulting Haematologist at the Royal Adelaide Hospital and one of the PACE trial investigators. “ICLUSIG will be a valuable new therapy for refractory leukaemia patients and treating clinicians in Australia.”

ARIAD submitted its marketing application for Iclusig in the third quarter of 2013 to the Therapeutics Goods Administration (TGA), in Australia. Commercial launch of ICLUSIG is expected to occur early in 2015.

“We are very pleased with the approval of ICLUSIG in Australia and will work

closely with STA to make Iclusig available to appropriate Philadelphia-positive leukaemia patients as quickly as possible," stated Harvey J. Berger, M.D., chairman and chief executive officer of ARIAD. "We look forward to continuing our strong collaboration with STA to provide this important treatment option to refractory CML patients in Australia."

"ICLUSIG provides a new treatment option for patients with difficult-to-treat CML or Ph+ ALL who previously had limited therapies available to them," said Carlo Montagner, chief executive officer at STA. "We look forward to the Pharmaceutical Benefit Advisory Committee's decision on ICLUSIG's reimbursement for Australian patients under the Pharmaceutical Benefits Scheme."

The TGA decision was based on results from the pivotal Phase 2 PACE (Ponatinib Ph+ ALL and CML Evaluation) trial in patients with CML or Ph+ ALL who were resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy, or who had the T315I mutation of BCR-ABL. ICLUSIG demonstrated anti-leukemic activity achieving a major cytogenetic response (MCyR) in 54 percent of chronic-phase CML patients and in 70 percent of patients with the T315I mutation.[1,2] MCyR within the first 12 months was the primary endpoint of the PACE trial for chronic-phase patients.[1,2]

In patients with advanced disease, 57 percent of accelerated-phase CML patients and 34 percent of blast-phase CML patients achieved a major hematologic response (MaHR) with Iclusig. MaHR within the first 6 months was the primary endpoint in the trial for patients with advanced disease.[1,2]

The most common (>1%) serious adverse reactions for Iclusig were pancreatitis, abdominal pain, decrease in platelet count, lipase increased, anaemia, cardiac failure, coronary artery disease, diarrhoea, decreased neutrophil count, febrile neutropenia, pancytopenia, and pyrexia.[2] The most common (≥20%) adverse reactions of any severity were decrease in platelet count, rash, dry skin, and abdominal pain.[2]

CML is a cancer of the white blood cells that is diagnosed in approximately 330 patients each year in Australia.[3] CML and Ph+ ALL patients treated with TKIs can

develop resistance or intolerance over time to these therapies. ICLUSIG is a targeted cancer medicine discovered and developed at ARIAD. It was designed by ARIAD scientists using ARIAD's platform of computational chemistry and structure-based drug design to inhibit BCR-ABL, including drug-resistant mutants that arise during treatment. ICLUSIG is the only TKI that has received an approval in Australia for an indication that includes CML and Ph+ ALL patients with the T315I mutation.

For further information, please consult the full ICLUSIG Product Information.

About CML and Ph+ ALL

CML is characterised by an excessive and unregulated production of white blood cells by the bone marrow due to a genetic abnormality that produces the BCR-ABL protein. After a chronic phase of production of too many white blood cells, CML typically evolves to the more aggressive phases referred to as accelerated phase and blast crisis. Ph+ ALL is a subtype of acute lymphoblastic leukaemia that carries the Ph+ chromosome that produces BCR-ABL. It has a more aggressive course than CML and is often treated with a combination of chemotherapy and tyrosine kinase inhibitors. The BCR-ABL protein is expressed in both of these diseases.

About ICLUSIG™ (ponatinib)

ICLUSIG is a kinase inhibitor. The primary target for Iclusig is BCR-ABL, an abnormal tyrosine kinase that is expressed in chronic myeloid leukemia (CML) and Philadelphia-chromosome positive acute lymphoblastic leukemia (Ph+ ALL). ICLUSIG was designed using ARIAD's computational and structure-based drug design platform specifically to inhibit the activity of BCR-ABL. ICLUSIG targets not only native BCR-ABL but also its isoforms that carry mutations that confer resistance to treatment, including the T315I mutation, which has been associated with resistance to other approved TKIs.

Minimum Product Information ICLUSIG™ (ponatinib HCl)

Indications: Adult patients with: Chronic phase, accelerated phase, or blast phase chronic myeloid Ieukaemia (CML) whose disease is resistant to, or who are intolerant of at least two prior tyrosine kinase inhibitors; or where there is a T3151mutation. Philadelphia chromosome positive acute lymphoblastic Ieukaemia (Ph+ ALL) whose disease is resistant to, or who are intolerant of dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate; or where there is a T3151 mutation. Therapy should be initiated and monitored by a haematologist with expertise in managing adult leukaemias. **Contraindications:** Hypersensitivity to ponatinib or excipients.

WARNING: VASCULAR OCCLUSION AND HEART FAILURE. Vascular Occlusion: Arterial and venous thrombosis and occlusions have occurred in at least 23% of ICLUSIG treated patients, including fatal myocardial infarction, stroke, stenosis of large arterial vessels of the brain, severe peripheral vascular disease, and the need for urgent revascularisation procedures. Patients with and without cardiovascular risk factors, including patients less than 50 years old, experienced these events. Monitor for evidence of thromboembolism and vascular occlusion. Interrupt or stop ICLUSIG immediately for vascular occlusion (see Precautions). Heart Failure, including fatalities, occurred in 8% of ICLUSIG-treated patients. Monitor cardiac function. Interrupt or stop ICLUSIG for new or worsening heart failure (see Precautions).

Precautions: Actively monitor and manage patients for vascular occlusions, cardiac failure, hypertension, haemorrhage, myelosuppression, hepatotoxicity, pancreatitis and QT prolongation before and during treatment. Interrupt, reduce or discontinue ICLUSIG as clinically indicated (see full PI). ***Vascular occlusion:*** Do not use if history of myocardial infarction, prior revascularisation or stroke, unless the benefit outweighs the risk. Monitor cardiovascular status and optimise therapy throughout. ***Cardiac failure:*** Monitor for heart failure and treat as clinically indicated. ***Hypertension:*** Monitor and treat hypertension to normalise blood pressure. ***Haemorrhage:*** including fatalities occurred. Mostly in patients with grade 4 thrombocytopaenia. ***Myelosuppression:*** Severe thrombocytopenia, neutropenia or anaemia. Perform complete blood counts every

2 weeks initially. ***Hepatotoxicity:*** Including severe drug induced liver injury and fatal hepatic failure. Monitor Liver Function Tests (LFT's) at baseline and at least monthly. ***Pancreatitis and serum lipase:*** Monitor serum lipase every 2 weeks initially. ***QT prolongation:*** QT prolongation seen with other BCR-ABL inhibitors. ***Lactose:*** contains lactose. ***Special populations:*** Caution or avoid in patients with moderate to severe hepatic impairment, pregnancy (category D), breastfeeding, the elderly, paediatric patients, driving or operating machinery (see full PI). ***Interactions with Other Medicines:*** Caution with concurrent strong CYP3A inhibitors, strong CYP3A inducers, substrates of P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) (see full PI). ***Adverse Effects:*** *Most common (≥ 20%) adverse drug reactions (ADRs)*: Platelet count decreased, rash, dry skin, and abdominal pain. *Most common (> 1%) serious ADRs*: Pancreatitis (5.1%), abdominal pain (1.8%), platelet count decreased (1.8%), lipase increased (1.3%), anaemia (1.3%), cardiac failure (1.3%), coronary artery disease (1.1%), diarrhoea (1.1%), neutrophil count decreased (1.1%), febrile neutropenia (1.1%), pancytopenia (1.1%), and pyrexia (1.1%). *Other very common (>10%) ADRs*: Upper respiratory tract infection, anaemia, neutrophil count decreased, decreased appetite, insomnia, headache, dizziness, hypertension, dyspnoea, cough, diarrhoea, vomiting, constipation, nausea, lipase increased, ALA increased, AST increased, bone pain, arthralgia, myalgia, pain in extremity, back pain, muscle spasms, fatigue, asthenia, oedema peripheral, pyrexia, pain. This is not a full list of adverse effects – refer to full PI for more information on common (>1%) and uncommon (>0.1%) ADRs. **Dosage and administration:** Monitor and manage cardiovascular risk factors before and throughout treatment. Dose: Starting dose, 45 mg once daily, with or without food. *Dose adjustments based on disease response*: Consider reducing the dose of ICLUSIG to 30 mg or 15 mg for chronic phase (CP) CML patients who have achieved a major cytogenetic response, especially in subjects at risk of vascular adverse events. Consider discontinuing ponatinib if a haematologic response has not occurred by 3 months (90 days) especially in subjects at risk of vascular adverse event. *Dose adjustments for toxicity*: Consider dose modification or treatment cessation to manage myelosuppression, vascular occlusion, uncontrolled hypertension, pancreatitis or elevated serum lipase and other severe adverse reactions. Provide haematologic support (platelet transfusion or haematopoietic growth factors) if clinically indicated.

About Specialised Therapeutics Australia

Specialised Therapeutics Australia Pty Ltd (STA) is a biopharmaceutical company dedicated to working with leading pharmaceutical companies worldwide to provide acute care therapies for high unmet medical needs to people living in Australia and New Zealand. The STA therapeutic portfolio and pipeline at present encompasses oncology, haematology, ophthalmology and infectious diseases. STA also has interests in the therapeutic areas of respiratory, dermatology, endocrinology and central nervous system (CNS).

About ARIAD

ARIAD Pharmaceuticals, Inc., headquartered in Cambridge, Massachusetts and Lausanne, Switzerland, is an integrated global oncology company focused on transforming the li

ves of cancer patients with breakthrough medicines. ARIAD is working on new medicines to advance the treatment of various forms of chronic and acute leukemia, lung cancer and other difficult-to-treat cancers. ARIAD utilises computational and structural approaches to design small-molecule drugs that overcome resistance to existing cancer medicines. For additional information, visit http://www.ariad.com or follow ARIAD on Twitter (@ARIADPharm).

This press release contains “forward-looking statements” which are based on management’s good-faith expectations and are subject to certain factors, risks and uncertainties that may cause actual results, outcome of events, timing and performance to differ materially from those expressed or implied by such statements. These factors, risks and uncertainties include, but are not limited to the Company’s ability to manufacture, and supply STA with Iclusig; the ability of STA to perform the contracted services, such as obtaining pricing and reimbursement approval for Iclusig in Australia; STA’s ability to distribute, promote, market and sell Iclusig in Australia; the timing and scope of the marketing authorisations, as well as the level of pricing obtained in Australia; third-party reimbursement; and the timing and success of sales of Iclusig in Australia. These factors, risks and uncertainties also include, but are not limited

to: the costs associated with ARIAD's development and manufacturing, commercial and other activities; the adequacy of capital resources and the availability of additional funding; and other factors detailed in the Company's public filings with the U.S. Securities and Exchange Commission. The information contained in this press release is believed to be current as of the date of original issue. After the date of this document, the Company does not intend to update any of the forward-looking statements to conform to actual results or to changes in the Company's expectations, except as required by law.

Reference:

1. Cortes JE, et al. N Engl J Med. 2013; 369:1783-96.
2. ICLUSIG (ponatinib) Approved Product Information.
3. Leukaemia Foundation, http://www.leukaemia.org.au/blood-cancers/leukaemias/chronic-myeloid-leukaemia-cml.