Aadi Bioscience Announces U.S. Commercial Launch and Availability of FYARRO™ for the Treatment of Adult Patients with Locally Advanced Unresectable or Metastatic Malignant PEComa

February 23, 2022

– FYARRO™ added to NCCN® Guidelines as the only preferred mTOR inhibitor to treat malignant PEComa –
– PRECISION-1 tumor agnostic study for TSC1 or TSC2 alterations is open for enrollment –

LOS ANGELES, Feb. 23, 2022 (GLOBE NEWSWIRE) -- Aadi Bioscience, Inc. ("Aadi") (Nasdaq: AADI), a biopharmaceutical company focusing on precision therapies for genetically-defined cancers with alterations in mTOR pathway genes, today announced the launch and commercial availability of its first proprietary product, FYARRO™ (sirolimus protein-bound particles for injectable suspension) (albumin-bound) for intravenous use for the treatment of adult patients with locally advanced unresectable or metastatic malignant PEComa. FYARRO was approved by the U.S. Food and Drug Administration (FDA) on November 22, 2021 and is the first treatment specific to this ultra-rare sarcoma. FYARRO was also recently added to the National Comprehensive Cancer Network® Clinical Practice Guidelines in Oncology (NCCN® Guidelines) as the only preferred treatment regimen for malignant PEComa.

"All of us at Aadi are truly proud to be able to offer this treatment to patients living with malignant PEComa, who have had no FDA-approved treatment options specific to this ultra-rare cancer until now. We are thankful to all the patients, families, and caregivers whose participation in and support of the AMPECT trial ultimately made this advancement possible," commented Neil Desai, Ph.D., Founder, President and Chief Executive Officer of Aadi. "We consider the availability of FYARRO in this indication an important advancement towards building out a potential 'pipeline within a product' and look forward to studying FYARRO in other tumor types with alterations in mTOR pathway genes. Our PRECISION-1 study, a registrational trial of FYARRO in patients with solid tumors with pathogenic alterations in *TSC1* or *TSC2* genes, is now open for enrollment," he added.

Aadi has also launched "Aadi Assist" as its comprehensive patient support program. This program offers resources designed to connect patients with co-pay assistance, referrals, educational resources, verification of benefits and to ensure access to this important drug as quickly and efficiently as possible.

Brendan Delaney, Chief Operating Officer of Aadi Bioscience, commented, "We have built a highly experienced commercial team and we are excited to launch Aadi's first product in the United States. We are committed to working with payers and healthcare providers across the country to help ensure access to FYARRO. We are also pleased that the NCCN® Sarcoma panel quickly included FYARRO as the only preferred regimen for malignant PEComa. This recommendation will help oncologists to make informed treatment decisions and will also accelerate patient access to therapy across the United States."

About NCCN®

The NCCN® is a not-for-profit alliance of 27 leading U.S. cancer centers devoted to patient care, research, and education, is dedicated to improving the quality, effectiveness, and efficiency of cancer care. The intent of the NCCN® Guidelines is to assist in the decision-making process of individuals involved in cancer care – including physicians, nurses, pharmacists, payers, patients, and their families – with the ultimate goal of improving patient care and outcomes. NCCN® recommended guidelines are listed by cancer types and FYARRO can be found within the Soft Tissue Sarcoma section within "Systemic Therapy Agents and Regimens with Activity in Soft Tissue Sarcoma Subtypes".

About Malignant PEComa

Advanced malignant PEComa, defined by the World Health Organization as 'mesenchymal tumors composed of distinctive cells that show a focal association with blood-vessel walls and usually express both melanocytic and smooth muscle markers,' are a rare subset of soft-tissue sarcomas, with an undefined cell of origin. While there is no formal epidemiology for malignant PEComa, it is estimated that there are about 100-300 new patients per year in the United States. Malignant PEComas may arise in almost any body site (typically the uterus, retroperitoneum, lung, kidney, liver, genitourinary, and gastrointestinal tract with a female predominance) and can have an aggressive clinical course including distant metastases and ultimately death. The estimated prognosis based on retrospective reports is 12-16 months. Cytotoxic chemotherapies typically used for sarcoma show minimal benefit. Malignant PEComas have been shown to frequently harbor alterations in the *TSC1* or *TSC2* genes that result in the activation of mTOR pathway thus making mTOR a rational therapeutic target for this disease.

About FYARRO™

FYARRO (sirolimus protein-bound particles for injectable suspension) (albumin-bound) is an mTOR inhibitor indicated for the treatment of adult patients with locally advanced unresectable or metastatic malignant perivascular epithelioid cell tumor (PEComa).

Important Safety Information

Contraindication

FYARRO is contraindicated in patients with a history of severe hypersensitivity to sirolimus, other rapamycin derivatives, or albumin.

Warnings and Precautions

Stomatitis

Stomatitis, including mouth ulcers and oral mucositis, occurred in 79% of patients treated with FYARRO, including 18% Grade 3. Stomatitis was most often first reported within 8 weeks of treatment. Based on the severity of the adverse reaction, withhold, resume at reduced dose, or permanently discontinue FYARRO.

Myelosuppression

FYARRO can cause myelosuppression including anemia, thrombocytopenia and neutropenia. Anemia occurred in 68% of patients; 6% were Grade 3. Thrombocytopenia and neutropenia occurred in 35% of patients each. Obtain blood counts at baseline and every 2 months for the first year of treatment and every 3 months thereafter, or more frequently if clinically indicated. Based on the severity of the adverse reaction, withhold, resume at reduced dose, or permanently discontinue FYARRO.

Infections

FYARRO can cause infections. Infections such as urinary tract infections (UTI), upper respiratory tract infections and sinusitis occurred in 59% of patients. Grade 3 infections occurred in 12% of patients, including a single case each of a UTI, pneumonia, skin, and abdominal infections. Monitor patients for infections, including opportunistic infections. Based on the severity of the adverse reaction, withhold, resume at reduced dose, or permanently discontinue FYARRO.

Hypokalemia

FYARRO can cause hypokalemia. Hypokalemia occurred in 44% of patients including 12% Grade 3 events. Monitor potassium levels prior to starting FYARRO and implement potassium supplementation as medically indicated. Based on the severity of the adverse reaction, withhold, resume at reduced dose, or permanently discontinue FYARRO.

Hyperglycemia

FYARRO can cause hyperglycemia. Hyperglycemia occurred in 12% of patients treated with FYARRO, all of which were Grade 3 events. Monitor fasting serum glucose prior to starting FYARRO. During treatment, monitor serum glucose every 3 months in non-diabetic patients, or as clinically indicated. Monitor serum glucose more frequently in diabetic patients. Based on the severity of the adverse reaction, withhold, resume at reduced dose, or permanently discontinue FYARRO.

Interstitial Lung Disease / Non-Infectious Pneumonitis

FYARRO can cause interstitial lung disease (ILD) / non-infectious pneumonitis. ILD / non-infectious pneumonitis occurred in 18% of patients treated with FYARRO, of which all were Grades 1 and 2. Based on the severity of the adverse reaction, withhold, reduce the dose, or permanently discontinue FYARRO.

Hemorrhage

FYARRO can cause serious and sometimes fatal hemorrhage. Hemorrhage occurred in 24% of patients treated with FYARRO, including Grade 3 and Grade 5 events in 2.9% of patients each. Monitor patients for signs and symptoms of hemorrhage. Based on the severity of adverse reaction, withhold, resume at reduced dose, or permanently discontinue FYARRO.

Hypersensitivity Reactions

FYARRO can cause hypersensitivity reactions. Hypersensitivity reactions, including anaphylaxis, angioedema, exfoliative dermatitis, and hypersensitivity vasculitis have been observed with administration of the oral formulation of sirolimus. Hypersensitivity reactions including anaphylaxis have been observed with human albumin administration. Monitor patients closely for signs and symptoms of infusion reactions during and following each FYARRO infusion in a setting where cardiopulmonary resuscitation medication and equipment are available. Monitor patients for at least 2 hours after the first infusion and as clinically needed for each subsequent infusion. Reduce the rate, interrupt infusion, or permanently discontinue FYARRO based on severity and institute appropriate medical management as needed.

Embryo-Fetal Toxicity

Based on animal studies and the mechanism of action, FYARRO can cause fetal harm when administered to a pregnant woman. In animal studies, mTOR inhibitors caused embryo-fetal toxicity when administered during the period of organogenesis at maternal exposures that were equal to or less than human exposures at the recommended lowest starting dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to avoid becoming pregnant and to use effective contraception while using FYARRO and for 12 weeks after the last dose.

Male Infertility

Azoospermia or oligospermia may be observed in patients treated with FYARRO. FYARRO is an anti-proliferative drug and affects rapidly dividing cells such as germ cells.

Immunizations and Risks Associated with Live Vaccines

No studies in conjunction with immunization have been conducted with FYARRO. Immunization during FYARRO treatment may be ineffective. Update immunizations according to immunization guidelines prior to initiating FYARRO, if possible. Immunization with live vaccines is not recommended during treatment and avoid close contact with those who have received live vaccines while on FYARRO. The interval between live vaccinations and initiation of FYARRO should be in accordance with current vaccination guidelines for patients on immunosuppressive therapies.

Risk of Transmission of Infectious Agents with Human Albumin

FYARRO contains human albumin, a derivative of human blood. Human albumin carries only a remote risk of transmission of viral diseases because of effective donor screening and product manufacturing processes. A theoretical risk for transmission of Creutzfeldt-Jakob Disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been associated with albumin.

Adverse Reactions

Adverse Reactions in PEComa

The most common adverse reactions (≥30%) were stomatitis in 27 (79%) patients; fatigue and rash in 23 (68%) patients each; infection in 20 (59%) patients; nausea and edema in 17 (50%) patients each; diarrhea, musculoskeletal pain and decreased weight in 16 (47%) patients each; decreased appetite in 15 (44%) patients; cough in 12 (35%) patients; and vomiting and dysgeusia in 11 (32%) patients each.

Laboratory Abnormalities in PEComa

The most common Grade 3 to 4 laboratory abnormalities (≥6%) were decreased lymphocytes in 7 (21%) patients; increased glucose and decreased potassium in 4 (12%) patients each; decreased phosphate in 3 (9%) patients; and decreased hemoglobin and increased lipase in 2 (6%) patients each.

Dosage interruptions

Dose interruptions of FYARRO due to an adverse reaction occurred in 22 (65%) patients. Adverse reactions which required dosage interruption in >5% of patients included stomatitis in 6 (18%) patients, pneumonitis in 5 (15%) patients, anemia in 3 (9%) patients, and dehydration, dermatitis acneiform, and thrombocytopenia in 2 (6%) patients each.

Dose reduction

Dose reductions of FYARRO due to an adverse reaction occurred in 12 (35%) patients. Adverse reactions which required dose reductions in > 5% of patients included stomatitis and pneumonitis in 3 (9%) patients each.

Drug Interactions

Reduce the dosage of FYARRO to 56 mg/m^2 when used concomitantly with a moderate or weak cytochrome P-450 3A4 (CYP3A4) inhibitor. Avoid concomitant use with drugs that are strong CYP3A4 and/or P-glycoprotein (P-gp) inhibitors and inducers and with grapefruit and grapefruit juice.

Use in Specific Populations

Pregnancy

Based on the mechanism of action and findings in animals, FYARRO can cause fetal harm when administered to a pregnant woman. Advise females of the potential risk to a fetus and to avoid becoming pregnant while receiving FYARRO.

Lactation

Sirolimus is present in the milk of lactating rats. There is potential for serious adverse effects from sirolimus in breastfed infants based on mechanism of action. Because of the potential for serious adverse reactions in breastfed infants from FYARRO, advise women not to breastfeed during treatment with FYARRO and for 2 weeks after the last dose.

Females and Males of Reproductive Potential

FYARRO can cause fetal harm when administered to a pregnant woman. Verify the pregnancy status of females of reproductive potential prior to starting treatment with FYARRO. Advise females of reproductive potential to use effective contraception and avoid becoming pregnant during treatment with and for at least twelve weeks after the last dose of FYARRO. Advise males with female partners of reproductive potential to use effective contraception and avoid fathering a child during treatment with FYARRO and for at least twelve weeks after the last dose of FYARRO. Although there are no data on the impact of FYARRO on fertility, based on available clinical findings with oral formulation of sirolimus and findings in animals, male and female fertility may be compromised by the treatment with FYARRO.

Pediatric

The safety and effectiveness of FYARRO in pediatric patients have not been established.

Geriatric Use

Of the 34 patients treated with FYARRO, 44% were 65 years of age and older, and 6% were 75 years of age and older. Clinical studies of FYARRO did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

Hepatic Impairment

FYARRO is not recommended for use in patients with severe hepatic impairment. Reduce FYARRO dosage in patients with mild or moderate hepatic impairment.

Full prescribing information can be found here.

About Aadi Bioscience

Aadi is a commercial-stage biopharmaceutical company focused on precision therapies for genetically-defined cancers. Aadi's primary goal is to bring transformational therapies to cancer patients with mTOR pathway driver alterations where other mTOR inhibitors have not or cannot be effectively

exploited due to problems of pharmacology, effective drug delivery, safety, or effective targeting to the disease site. In November 2021, Aadi received FDA approval for FYARRO for the treatment of adult patients with locally advanced unresectable or metastatic malignant perivascular epithelioid cell tumor (PEComa). FYARRO is an mTOR inhibitor bound to human albumin that has demonstrated significantly higher tumor accumulation, greater mTOR target suppression, and increased tumor growth inhibition over other mTOR inhibitors in preclinical models.

Based on data from the AMPECT trial with FYARRO and following discussions with the FDA about other emerging data with FYARRO, Aadi has initiated PRECISION 1, a tumor-agnostic registrational trial in mTOR inhibitor-naïve solid tumors harboring *TSC1* or *TSC2* inactivating alterations. Aadi also has ongoing studies to evaluate dosing of FYARRO in combination regimens. More information on Aadi's development pipeline is available on the Aadi website at www.aadibio.com.

Forward-Looking Statements

Aadi cautions you that certain statements included in this press release that are not a description of historical facts are forward-looking statements. These statements are based on Aadi's current beliefs and expectations. Forward-looking statements include statements regarding: our plans and potential for success relating to commercializing FYARRO, the expectations regarding the beneficial characteristics, safety, efficacy and therapeutic effects of FYARRO, our plans related to further development and manufacturing of FYARRO, the timing of additional clinical trials, including the registrational trial in patients harboring *TSC1* and *TSC2* inactivating alterations, the timing or likelihood of regulatory filings and approvals of FYARRO, including in potential additional indications and potential filings in additional jurisdictions, anticipated reception of FYARRO in the physician community, and the sufficiency of our existing capital resources to fund our future operating expenses and capital expenditure requirements. Actual results could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation: risks related to Aadi's ability to successfully commercialize; uncertainties associated with the clinical development and regulatory approval of FYARRO, including potential delays in the commencement, enrollment and completion of clinical trials for additional indications; the risk that interim results of clinical trials may not be reproduced and do not necessarily predict final results; the risk that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, and as more patient data become available; the risk that unforeseen adverse reactions or side effects may occur in the course of commercializing, developing and testing FYARRO; risks associated with the failure to realize any value from FYARRO in light of inherent risks and difficulties involved in successfully bringing product candidates to market; risks related to Aadi's estimates regarding future expenses, capital requirements and need for additional financing; and risks related to the impact of the COVID-19 outbreak on Aadi's operations, the biotechnology industry and the economy generally.

Additional risks and uncertainties that could cause actual outcomes and results to differ materially from those contemplated by the forward-looking statements are included under the caption "Risk Factors" in Aadi's Form 10-Q filed on November 10, 2021, and elsewhere in Aadi's reports and other documents that Aadi has filed, or will file, with the SEC from time to time and available at www.sec.gov.

All forward-looking statements in this press release are current only as of the date hereof and, except as required by applicable law, Aadi undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise. All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

FYARRO™ is a trademark of Aadi Bioscience, Inc.

For more information about FYARRO, visit: https://fyarro.com/

For more information about Aadi Assist, go to: http://aadiassist.com/.

For more information about the National Comprehensive Cancer Network, go to:

https://www.nccn.org/home/about

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