Aadi Bioscience Announces Exploratory Biomarker Data from Patients in Its AMPECT Trial and Expanded Access Program to be Presented at 2022 ASCO Annual Meeting

May 26, 2022

Target tumor reductions observed in advanced malignant PEComa patients harboring TSC1 or TSC2 inactivating alterations regardless of prior mTOR inhibitor exposure

LOS ANGELES, May 26, 2022 (GLOBE NEWSWIRE) -- Aadi Bioscience, Inc. (NASDAQ: AADI), a biopharmaceutical company focused on developing and commercializing precision therapies for genetically defined cancers with alterations in mTOR pathway genes, today announced presentation of a poster entitled, "*nab*-Sirolimus for patients with advanced malignant PEComa with or without prior mTOR inhibitors: Biomarker results from AMPECT and an expanded access program" at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting, being held online and in person from June 3-7 in Chicago, IL.

The data represent exploratory biomarker results reported from the final analysis of mTOR inhibitor-naïve advanced malignant PEComa patients treated with *nab*-sirolimus in Aadi's Advanced Malignant PEComa Trial (AMPECT) trial as well as an analysis of prior mTOR inhibitor exposed advanced malignant PEComa patients treated with nab-sirolimus in the Expanded Access Program (EAP) through June 2021. While the AMPECT and EAP studies cannot be directly compared, the findings of each show a greater clinical benefit in the patients harboring *TSC1* or *TSC2* alterations who received *nab*-sirolimus compared to all evaluable patients, regardless of prior mTOR inhibitor exposure.

"Given that inactivating alterations in *TSC1* or *TSC2* are potentially targetable biomarkers for mTOR inhibition, the exploratory biomarker results from these studies are encouraging as they support the rationale for our ongoing PRECISION 1 Phase 2 registrational trial," said Neil Desai, Ph.D., Founder, President and Chief Executive Officer of Aadi. "The response rates to *nab*-sirolimus in both AMPECT and the EAP showed similar positive trends in patients with *TSC1* or *TSC2* alterations, regardless of prior mTOR inhibitor exposure."

Nab-sirolimus is an albumin-bound mTOR inhibitor approved by the U.S. Food and Drug Administration (FDA) as FYARRO™ for the treatment of adult patients with locally advanced unresectable or metastatic malignant PEComa. The data to be presented include 31 mTOR inhibitor naïve patients from the AMPECT trial and 16 patients with prior mTOR inhibitor treatment from the EAP, all of which were treated with *nab*-sirolimus. Of those patients with *TSC1* or *TSC2* alterations in the AMPECT trial, 64% had a complete or partial response versus a 39% response rate for all evaluable patients in the trial. Of those patients with *TSC1* or *TSC2* alterations in the EAP, 44% had a partial response versus 25% for all evaluable patients in the program.

Presentation details:

Abstract Title:	"*nab*-Sirolimus for patients with advanced malignant PEComa with or without prior mTOR inhibitors: Biomarker results from AMPECT and an expanded access program" (Dickson, et al.)
Abstract Number:	11574
Session Title:	Sarcoma
Session Date:	Sunday, June 5, 2022
Session Time:	6 am ET/9am PT
Presenter:	Mark Andrew Dickson, MD

About the AMPECT Trial

The AMPECT trial (NCT02494570) evaluated the efficacy and safety of *nab*-sirolimus and was the first prospective registrational study in advanced malignant PEComa. AMPECT was a Phase 2, open-label, single-arm, multi-center study in patients with advanced malignant PEComa to determine the efficacy and safety of *nab*-sirolimus (data cutoff as of June 2021). Data from this trial were the basis of the FDA approval of FYARRO™ in advanced malignant PEComa.

In the trial, the overall response rate as assessed by independent review was 39% (12/31), with 2 patients converting from a Partial Response to a Complete Response after prolonged follow up. The median duration of response has not been reached with a median follow-up of 36 months, and a range of 5.6 to 55.5+ months and ongoing. Among responders, 92% had a response lasting greater than or equal to 6 months; 67% had a response lasting greater than or equal to 12 months; and 58% had a response lasting greater than or equal to 2 years. As is the case with other therapeutics of the mTOR class, the FYARRO prescribing information includes warnings and precautions related to stomatitis, myelosuppression, infections, hypokalemia, hyperglycemia, interstitial lung disease/non-infectious pneumonitis, hemorrhage, and hypersensitivity reactions. Grade 3 non-hematologic events occurring in ≥ 10% of patients included stomatitis, rash, fatigue and infections. Grade 3 laboratory abnormalities occurring in ≥ 10% of patients that worsened from baseline included lymphocytopenia, increased glucose, and decreased potassium.

About the Aadi Expanded Access Program (EAP) for *nab*-sirolimus

Between closure of the AMPECT trial and *nab*-sirolimus commercial availability, an expanded access program (EAP; NCT03817515) allowed for the

treatment of advanced malignant PEComa patients as well as other malignancies with relevant genetic mutations or mTOR pathway activation.

Amongst the patients on the EAP, sixteen with advanced malignant PEComa and prior mTOR inhibitor exposure were treated from July 2019 to July 2021. Prior mTOR inhibitor treatments included sirolimus, everolimus, temsirolimus and sapanisertib. Twelve patients had exposure to one prior mTOR inhibitor and four patients had exposure to >2 prior mTOR inhibitors. Fifty percent had progressive disease as best response on previous mTOR inhibitor treatment. Adverse events reported by treating physicians in the EAP were consistent with what was reported in AMPECT.

For detailed important safety information, please see below.

About FYARRO ™

FYARRO 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 the PRECISION 1 Trial

The PRECISION 1 trial is a multi-center, open-label, tumor-agnostic pivotal study, of *nab*-sirolimus designed as a basket trial that will evaluate approximately 120 adult and adolescent patients with solid tumors harboring pathogenic inactivating alterations in *TSC1* or *TSC2* genes. The trial will have two independent arms of 60 patients each to separately evaluate patients with either *TSC1* or *TSC2* inactivating alterations. Aadi has received Fast Track designation to evaluate *nab*-sirolimus in this indication from the FDA. The first patient in the PRECISION 1 trial was dosed in March 2022.

About Aadi Bioscience

Aadi is a 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), and in February 2022 Aadi announced the commercial launch of FYARRO in this indication.

Based on data from Aadi's Phase 2 registrational study, AMPECT, with FYARRO, and, following discussions with the FDA about other emerging data with FYARRO, Aadi has initiated PRECISION 1, a Phase 2 tumor-agnostic registration-directed trial in mTOR inhibitor-naïve solid tumors harboring *TSC1* or *TSC2* inactivating alterations. To learn more, visit www.aadibio.com and connect with us on Twitter and LinkedIn.

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; anticipated reception of FYARRO in the physician community; the results and timing of additional clinical trials, including the registration-directed trial in patients harboring *TSC1* or *TSC2* inactivating alterations, the timing and likelihood of regulatory filings and approvals of FYARRO, including in potential additional indications and potential filings in additional jurisdictions; and the sufficiency of our existing capital resources and the expected timeframe 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 uncertainties associated with the clinical development and regulatory approval of FYARRO in additional indications, including potential delays in the commencement, enrollment and completion of clinical trials for additional indications; the risk that unforeseen adverse reactions or side effects may occur in the course of commercializing, developing and testing FYARRO; Aadi's continued reliance on third parties to conduct additional clinical trials of 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;; and risks related to the impact of the COVID-19 pandemic 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 May 12, 2022, 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.

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