Fyarro™ (sirolimus protein-bound particles) (albumin-bound) – New orphan drug approval

- On November 23, 2021, Aadi Bioscience announced the FDA approval of Fyarro (sirolimus protein-bound particles) (albumin-bound), for the treatment of adult patients with locally advanced unresectable or metastatic malignant perivascular epithelioid cell tumor (PEComa).

- Advanced malignant PEComa are a rare subset of soft-tissue sarcomas, with an undefined cell of origin. There are about 100 to 300 new patients per year in the U.S.

- Fyarro is the first approved drug for advanced malignant 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.

- The efficacy of Fyarro was established in AMPECT, a single-arm study in 31 patients with locally advanced unresectable or metastatic malignant PEComa. Patients received Fyarro until disease progression or unacceptable toxicity. The major efficacy outcome measures were overall response rate (ORR) and duration of response (DOR).

    — The ORR was 39% (95% CI: 22, 58).
    — The median DOR was not reached (6.5, not estimable).

- Warnings and precautions for Fyarro include stomatitis; myelosuppression; infections; hypokalemia; hyperglycemia; interstitial lung disease / non-infectious pneumonitis; hemorrhage hypersensitivity reactions; embryo-fetal toxicity; male infertility; immunizations and risks associated with live vaccines; and risk of transmission of infectious agents with human albumin.

- The most common adverse reactions (≥ 30%) with Fyarro use were stomatitis, fatigue, rash, infection, nausea, edema, diarrhea, musculoskeletal pain, decreased weight, decreased appetite, cough, vomiting, and dysgeusia.

- The most common grade 3 to 4 laboratory abnormalities (≥ 6%) with Fyarro use were decreased lymphocytes, increased glucose, decreased potassium, decreased phosphate, decreased hemoglobin, and increased lipase.

- The recommended dosage of Fyarro is 100 mg/m^2 administered as an intravenous infusion over 30 minutes on days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity.

- Aadi Bioscience plans to launch Fyarro in the first quarter of 2022. Fyarro will be available as a lyophilized powder containing 100 mg of sirolimus formulated as albumin-bound particles in single-dose vial for reconstitution.