AVEO Oncology Highlights Recent Progress and 2022 Outlook

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BOSTON, Jan. 04, 2022 (GLOBE NEWSWIRE) -- AVEO Oncology (Nasdaq: AVEO), a commercial stage, oncology-focused biopharmaceutical company, today highlighted its recent progress and outlook for 2022.

"I am proud of the entire AVEO team this year, as we accomplished several key milestones in the face of what remains a challenging environment with the ongoing COVID-19 pandemic," said Michael Bailey, President and Chief Executive Officer of AVEO. "Our commercial team has executed our go-to-market strategy for FOTIVDA® (tivozanib) with tenacity since we launched at the end of March 2021. We are focused on our goal of continuing to deliver quarter over quarter growth, and we expect that the sales ramp should continue to increase even as we persevere through the COVID-19 environment. Our team continues to enhance their outreach methods to educate oncologists about the TIVO-3 data that demonstrate FOTIVDA's robust efficacy and favorable tolerability profile in patients with relapsed or refractory (R/R) renal cell carcinoma (RCC)."

Mr. Bailey added: "In addition to our progress with FOTIVDA's launch, we continue to be pleased by the progress the team is making in advancing the development of our clinical pipeline, with a number of key milestones announced throughout 2021 that we believe represent significant opportunities to build long-term shareholder value in 2022 and beyond. For tivozanib, these milestones include initiation and continued enrollment of the Phase 3 TiNivo-2 clinical trial in advanced refractory RCC, and the presentation of data for the first-line cohort of the Phase 1b/2 DEDUCTIVE clinical trial in unresectable locally advanced or metastatic hepatocellular carcinoma (HCC) at American Society of Clinical Oncology (ASCO) GI. For ficlatuzumab, we have initiated the scale up for the manufacturing run expected in the second quarter of 2022, we recently announced a supply agreement with Merck KGaA, and we gained Fast Track designation from the U.S. FDA for the investigation of ficlatuzumab and ERBITUX® (cetuximab) for the treatment of patients with relapsed or recurrent head and neck squamous cell carcinoma (r/r HNSCC). These milestones position us well for a potential registrational trial that is expected to start in 2023. In addition, we completed the Phase 1 clinical trial in healthy volunteers for AV-380 and expect to present results in mid-year 2022 and plan to initiate the Phase 1b clinical trial for this program in cancer patients at that time. In summary, we believe this progress is further proof of our team's ability to execute and develop therapies that address high patient need."

Key Recent Program Updates and Anticipated 2022 Milestones

FOTIVDA® (tivozanib) Update

- **Successfully Launched U.S. Commercialization Team for FOTIVDA.** The team executed the U.S. commercial build out by hiring and training field teams and building infrastructure – including distribution, patient access and securing broad reimbursement. Market penetration for FOTIVDA has continued to increase since its commercial launch at the end of March 2021. Feedback from the field team suggests FOTIVDA has been well received by oncologists treating r/r RCC, noting both the durable responses and tolerability profile they have observed as attractive for their third-line patients.

  As with other launches during the COVID-19 pandemic, the sales team's access to oncologists and their staff has been limited which the Company believes has potentially slowed the launch trajectory. This headwind continued in the fourth quarter of 2021 with the emergence of the Delta and Omicron COVID-19 variants. Despite these access challenges, AVEO expects to have continued quarter over quarter net revenue and underlying prescription demand growth in the fourth quarter of 2021. In addition, as is typical with launches in the relapsed/refractory oncology setting, physicians will tend to prescribe newly approved therapies for later line patients and, following positive experience with a new therapy, will prescribe to earlier line patients. To date, the majority of the patients prescribed FOTIVDA have been 4th line or later. We expect later line patients to generally exhibit higher early discontinuation rates. With slower account access due to COVID-19 related restrictions, the Company believes that broad product adoption in earlier lines of treatment may continue to be protracted. AVEO continues to believe FOTIVDA has the potential to become a standard of care for patients that have received two or more prior systemic treatments.

- **Data from a long-term efficacy follow-up and additional tolerability analyses from the TIVO-3 trial comparing tivozanib to sorafenib in r/r advanced RCC following two or more prior systemic therapies were presented at the ASCO 2021 Annual Meeting.** These data included updated durability of response (DOR) and overall survival (OS) results, as well as an analysis of treatment-emergent adverse events (TEAEs) across trial arms.
  - Tivozanib demonstrated clinically meaningful and statistically significant improvements in overall response rate (ORR) and DOR compared to sorafenib in highly relapsed or refractory RCC patients in the TIVO-3 trial. In addition, the long-term OS relative to sorafenib continued to improve with a hazard ratio of 0.91, as presented at ASCO 2021.

- Patients in the TIVO-3 trial demonstrated a longer duration of treatment exposure with tivozanib than sorafenib (11.9 cycles vs. 6.7 cycles), but fewer all-grade and grade ≥3 TEAEs. The observed TEAEs were generally similar with tivozanib and sorafenib. Patients receiving tivozanib in the TIVO-3 trial required fewer dose reductions, and the time to dose reductions were longer with tivozanib than sorafenib.

- **Data from a key subgroup and quality of life analyses from the Phase 3 TIVO-3 study of tivozanib in RCC presented at the ASCO 2021 Genitourinary (GU) Cancers 2021 Symposium.**
  - Data highlighting outcomes of the subgroup of TIVO-3 patients who received tivozanib following prior axitinib therapy suggests that tivozanib, a potent and selective vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitor (TKI), is more active following prior VEGFR TKI therapy than sorafenib, a multi-targeted VEGFR TKI.
  - Tivozanib demonstrated significantly increased quality-adjusted time without symptoms of disease and toxicity (QTWiST) relative to sorafenib as third- or fourth-line therapy in patients with RCC.

- **Initiation of the Phase 3 TiNivo-2 trial evaluating the combination of r tivozanib and OPDIVO®.** A Phase 3 clinical trial of tivozanib in combination with Bristol-Myers Squibb's OPDIVO ® (nivolumab), an antibody directed against programmed death-1 (PD-1), versus tivozanib monotherapy for the treatment of RCC patients progressing after one or two lines of prior therapy, one of which must include immunotherapy, opened for enrollment during the third quarter of 2021.

- **Completed enrollment in the first-line cohort of the ongoing Phase 1b/2 DEDUCTIVE trial.** This is a study of tivozanib in combination with IMFINZI® (durvalumab), AstraZeneca's human monoclonal antibody directed against programmed death-ligand 1 (PD-L1), in patients with unresectable locally advanced or metastatic HCC. The trial has completed enrollment of the first-line cohort and is currently enrolling a second cohort of patients after pre-treatment with bevacizumab and atezolizumab in a prior line of therapy. The Company expects to present the data from the first-line cohort at ASCO GI in January 2022.

Ficlatuzumab Update

- **Presented positive data from the Phase 2 clinical trial of ficlatuzumab alone or in combination with cetuximab in pan-refractory HNSCC at the 2021 ASCO Annual Meeting.** Data from the portion of the trial that included patients with HPV negative disease, a subgroup of metastatic HNSCC normally associated with poorer outcomes, who received the combination of ficlatuzumab and cetuximab demonstrated improved responses, including two patients with complete responses, which compares favorably to historical controls.

- **Based on the Phase 1b and Phase 2 clinical trial results, ficlatuzumab was granted Fast Track Designation by the U.S. FDA for the evaluation of ficlatuzumab in combination with Erbitux (cetuximab) for the treatment of patients with r/r HNSCC.**

- **Announced plans to initiate a potential registrational Phase 3 clinical trial for ficlatuzumab in HPV negative HNSCC in the first half of 2023**.
  - AVEO has begun the manufacturing scale up and expects to commence manufacturing of ficlatuzumab clinical supply in the second quarter of 2022.
  - In support of the proposed HPV negative HNSCC Phase 3 clinical trial of ERBITUX® (cetuximab) and ficlatuzumab, AVEO recently entered into a clinical trial collaboration and supply agreement for ERBITUX for the EU study sites with Merck KGaA, Darmstadt, Germany.
  - AVEO expects to continue to discuss potential ficlatuzumab registrational clinical trial designs with the FDA and with potential partners.

AV-380 Update

- AV-380 is a first-in-class, potent, humanized inhibitory IgG1 monoclonal antibody targeting growth differentiation factor 15 (GDF15), a potential treatment pathway for cancer and/or cachexia.
- The last patient has been dosed in the Phase 1 clinical trial of AV-380 in healthy volunteers. AVEO expects to present data from the Phase 1 clinical trial in mid-2022 at a scientific meeting.
- AVEO plans to initiate a Phase 1b clinical trial in cancer patients in mid-2022.

AV-203 Update

- During 2021, AVEO regained worldwide rights to AV-203. AV-203 is a clinical-stage potent humanized IgG1 monoclonal antibody that targets ErbB3 (also known as HER3). AV-203 has demonstrated preclinical activity in a number of different tumor models, including breast, head and neck, lung, ovarian and pancreatic cancers.

Corporate Updates

- **Kevin Cullen, M.D. appointed to Board of Directors.** AVEO appointed Dr. Cullen to its Board of Directors in April of 2021. A widely recognized clinical oncologist with a specialty in head and neck cancer, Dr. Cullen is the Marlene and Stewart Greenebaum Distinguished Professor in Oncology and director of the Program in Oncology at the University of Maryland School of Medicine. He also serves as director of the University of Maryland Marlene and Stewart Greenebaum Comprehensive Cancer Center.
- **Jeb Ledell Appointed as Chief Operating Officer.** AVEO appointed Mr. Ledell as chief operating officer in December 2021, where he is responsible for overseeing operational functions key to maximizing AVEO's organizational efficiency and advancing its pipeline of products. Mr. Ledell joins AVEO from Enzyvant Therapeutics, where he served as chief operating officer and led key business operations during the recent FDA approval of RETHYMIC®. Prior to Enzyvant, Mr. Ledell served as the chief operating officer at Compass Therapeutics and Horizon Discovery Group, during which time he led operations at both organizations through several changes in scale.
- **Additional $5.0 million made available to the Company under its 2020 Loan Facility with Hercules Capital, Inc. (Hercules) and its affiliates**. In late December 2021, the Company achieved sales Performance Milestone II of $35.0 million in net product revenues from sales of FOTIVDA ahead of the April 1, 2022 deadline. The Company drew down the additional $5.0 million tranche in 2021.

About FOTIVDA® (tivozanib)

FOTIVDA® (tivozanib) is an oral, next-generation vascular endothelial growth factor receptor (VEGFR) tyrosine kinase inhibitor (TKI). It is a potent, selective inhibitor of VEGFRs 1, 2, and 3 with a long half-life designed to improve efficacy and tolerability. AVEO received U.S. Food and Drug Administration (FDA) approval for FOTIVDA on March 10, 2021 for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies. FOTIVDA was approved in August 2017 in the European Union and other countries in the territory of its partner EUSA Pharma (UK) Limited for the treatment of adult patients with advanced RCC. FOTIVDA has been shown to significantly reduce regulatory T-cell production in preclinical models.[2] FOTIVDA was discovered by Kyowa Kirin.

INDICATIONS

FOTIVDA is indicated for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma (RCC) following two or more prior systemic therapies.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypertension and Hypertensive Crisis: Control blood pressure prior to initiating FOTIVDA. Monitor for hypertension and treat as needed. For persistent hypertension despite use of anti-hypertensive medications, reduce the FOTIVDA dose.

Cardiac Failure: Monitor for signs or symptoms of cardiac failure throughout treatment with FOTIVDA.

Cardiac Ischemia and Arterial Thromboembolic Events: Closely monitor patients who are at increased risk for these events. Permanently discontinue FOTIVDA for severe arterial thromboembolic events, such as myocardial infarction and stroke.

Venous Thromboembolic Events: Closely monitor patients who are at increased risk for these events. Permanently discontinue FOTIVDA for severe venous thromboembolic events.

Hemorrhagic Events: Closely monitor patients who are at risk for or who have a history of bleeding.

Proteinuria: Monitor throughout treatment with FOTIVDA. For moderate to severe proteinuria, reduce the dose or temporarily interrupt treatment with FOTIVDA.

Thyroid Dysfunction: Monitor before initiation and throughout treatment with FOTIVDA.

Risk of Impaired Wound Healing: Withhold FOTIVDA for at least 24 days before elective surgery. Do not administer for at least 2 weeks following major surgery and adequate wound healing. The safety of resumption of FOTIVDA after resolution of wound healing complications has not been established.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): Discontinue FOTIVDA if signs or symptoms of RPLS occur.

Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception.

Allergic Reactions to Tartrazine: The 0.89 mg capsule of FOTIVDA contains FD&C Yellow No.5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible patients.

ADVERSE REACTIONS

The most common (≥20%) adverse reactions were fatigue, hypertension, diarrhea, decreased appetite, nausea, dysphonia, hypothyroidism, cough, and stomatitis, and the most common Grade 3 or 4 laboratory abnormalities (≥5%) were sodium decreased, lipase increased, and phosphate decreased.

DRUG INTERACTIONS

Strong CYP3A4 Inducers: Avoid coadministration of FOTIVDA with strong CYP3A4 inducers.

USE IN SPECIFIC POPULATIONS

Lactation: Advise not to breastfeed.
Females and Males of Reproductive Potential: Can impair fertility.
Hepatic Impairment: Adjust dosage in patients with moderate hepatic impairment. Avoid use in patients with severe hepatic impairment.

To report SUSPECTED ADVERSE REACTIONS, contact AVEO Pharmaceuticals, Inc. at 1-833-FOTIVDA (1-833-368-4832) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see FOTIVDA Full Prescribing Information which is available at www.FOTIVDA.com.

About Advanced Renal Cell Carcinoma

According to the American Cancer Society's 2021 statistics, renal cell carcinoma (RCC) is the most common type of kidney cancer, which is among the ten most common cancers in both men and women. Approximately 73,750 new cases of kidney cancer will be diagnosed annually and about 14,830 people will die from this disease. In patients with late-stage disease, the five-year survival rate is 13%. Agents that target the vascular endothelial growth factor (VEGF) pathway have shown significant antitumor activity in RCC.[3] According to a 2019 publication, 50% of the approximately 10,000 patients who progress following two or more lines of therapy choose not to receive further treatment,[4] which may be attributable to tolerability concerns and a lack of data to support evidence-based treatment decisions in this highly relapsed or refractory patient population.

About AVEO Pharmaceuticals, Inc.

AVEO is a commercial-stage, oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for patients with cancer. AVEO currently markets FOTIVDA® (tivozanib) in the United States for the treatment of adult patients with relapsed or refractory renal cell carcinoma (RCC) following two or more prior systemic therapies. AVEO continues to develop FOTIVDA in immuno-oncology combinations in RCC and other indications, and has other investigational programs in clinical development. AVEO is committed to creating an environment of diversity, equity and inclusion to diversify representation within the Company.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements of AVEO within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this press release are forward-looking statements. The words "anticipate," "believe," "design," "expect," "hope," "intend," "may," "plan," "potential," "could," "should," "would," "seek," "look forward," "advance," "goal," "strategy," or the negative of these terms or other similar expressions, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among others, statements about: AVEO's expectations of achieving quarter over quarter sales growth and an increase in its sales ramp of FOTIVDA in future periods; AVEO's plans, strategies and ability to successfully commercialize, sell and distribute FOTIVDA to patients in the United States; the potential for FOTIVDA as a treatment option for patients with relapsed or refractory advanced RCC; the potential efficacy, safety and tolerability of tivozanib, both as a stand-alone drug candidate and in combination with other therapies in other indications; AVEO's plans, strategies and execution for current and future clinical trials of tivozanib, ficlatuzumab and AV-380; the advancement of AVEO's pipeline, including the advancement of tivozanib (in additional indications), ficlatuzumab and AV-380 in multiple clinical studies; the timing of delivery and availability of clinical supplies of ficlatuzumab; the timing and execution of the potential registrational clinical trial of ficlatuzumab in HPV negative patients with HNSCC; the potential efficacy, safety and tolerability of ficlatuzumab, both as a stand-alone drug candidate and in combination with other therapies in HPV negative HNSCC and other indications; the potential clinical utility of ficlatuzumab and AV-380 in areas of unmet need; AVEO's strategy, prospects, plans and objectives for FOTIVDA and its product candidates and for AVEO generally; the potential outcomes from studies of its product candidates to provide AVEO with opportunities to pursue regulatory strategies; the potential commercial opportunity of FOTIVDA and AVEO's other product candidates; the period in which AVEO expects to have cash to fund its operations; and AVEO's estimates for its cash runway and the contingencies on which such runway is dependent. AVEO has based its expectations and estimates on assumptions that may prove to be incorrect. As a result, readers are cautioned not to place undue reliance on these expectations and estimates. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that AVEO makes due to a number of important factors, including risks relating to: AVEO's ability to achieve quarter over quarter sales growth of FOTIVDA; the ongoing access challenges arising from the COVID-19 pandemic and related variants; the percentage of FOTIVDA prescriptions being made to patients who are beyond the third- and fourth-line treatment setting maintaining or increasing over time; AVEO's ability to successfully implement its strategic plans, including its ability to successfully commercialize FOTIVDA and to obtain and maintain market and third party payor acceptance of FOTIVDA; AVEO's ability, and the ability of its licensees, to demonstrate to the satisfaction of applicable regulatory agencies such as the FDA the safety, efficacy and clinically meaningful benefit of AVEO's product candidates, and risks relating to the timing and costs of seeking and obtaining regulatory approvals; AVEO's dependence on third-party vendors for the development, manufacture, supply, storage and distribution of FOTIVDA, ficlatuzumab and its other product candidates; AVEO's ability to enter into and maintain its third party collaboration and license agreements, and its ability, and the ability of its strategic partners, to achieve development and commercialization objectives under these arrangements; AVEO's and its collaborators' ability to successfully enroll and complete clinical trials; AVEO's ability to maintain compliance with regulatory requirements applicable to FOTIVDA and its product candidates; AVEO's ability to obtain sufficient clinical supplies of its product candidates; AVEO's ability to obtain and maintain adequate protection for intellectual property rights relating to FOTIVDA and its other product candidates; unplanned capital requirements; uncertainties related to AVEO's ability to access future borrowings under the Hercules loan agreement, which turns on the achievement of milestones related to sales of FOTIVDA in the U.S., which milestones may not be achieved; adverse general economic, political and industry conditions; the potential adverse effects of the COVID-19 pandemic on AVEO's business continuity, financial condition, results of operations, liquidity and ability to commercialize FOTIVDA, manufacture clinical and commercial product and timely initiate new clinical trials or complete its ongoing clinical trials; competitive factors; and those risks discussed in the sections titled "Risk Factor Summary," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources" included in AVEO's quarterly and annual reports on file with the Securities and Exchange Commission (SEC) and in other filings that AVEO makes with the SEC. The forward-looking statements in this press release represent AVEO's views as of the date of this press release, and subsequent events and developments may cause its views to change. While AVEO may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. You should, therefore, not rely on these forward-looking statements as representing AVEO's views as of

any date other than the date of this press release.

Any reference to AVEO's website address in this press release is intended to be an inactive textual reference only and not an active hyperlink.

References

1. Fotivda (Tivozanib) USPI March 2021
2. Fotivda (Tivozanib) SmPC August 2017
3. Motzer RJ, Nosov D, Eisen T, et al. J Clin Oncol 2013; 31(30): 3791-9
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