Acrivon Therapeutics Reports Positive Endometrial Cancer Data from Ongoing ACR-368 Registrational Intent Phase 2 Study at ESMO, Advancement of ACR-2316 into Clinic Ahead of Timelines, and Progress on its AP3 Interactome for Proprietary Data Analysis

September 14, 2024

- *Confirmed overall response rate (ORR) = 62.5% (95% CI, 30.4-86.5) observed in prospectively-selected ACR-368 OncoSignature-positive (BM+) patients with endometrial cancer*
- *Achieved statistically significant segregation of responders in BM+ vs BM- subgroups based on OncoSignature patient selection (p-value = 0.009)*
- *ACR-368 endometrial cohort data maturing with all responders still on therapy; mDoR not yet reached (~6 months at time of data-cut)*
- *Endometrial cancer now anticipated to be the first tumor type with potential for ACR-368 accelerated regulatory approval*
- *IND clearance and initial sites activated ahead of timelines for ACR-2316 with first-in-human dosing anticipated in Q4 2024*
- *AP3 Interactome generating proprietary, actionable insights, leveraging in-house data and delivering algorithm-based machine learning-enabled pathway and biomarker analyses*
- *Acrivon to host a webcast joined by endometrial cancer key opinion leader Dr. Ramez N. Eskander today, Saturday, September 14 at 9:00 a.m. ET*

WATERTOWN, Mass., Sept. 14, 2024 (GLOBE NEWSWIRE) -- Acrivon Therapeutics, Inc. (“Acrivon” or “Acrivon Therapeutics”) (Nasdaq: ACRV), a clinical stage precision medicine company utilizing its Acrivon Predictive Precision Proteomics (AP3) platform for the discovery, design, and development of drug candidates through a mechanistic match to patients whose disease is predicted sensitive to the specific treatment, today presented additional positive clinical data at ESMO from the ongoing registrational intent, multicenter Phase 2 trial of ACR-368 in patients with locally advanced or metastatic, recurrent endometrial cancer. The company has also disclosed that the Investigational New Drug (IND) application for its next clinical candidate, ACR-2316, has been cleared by the FDA with initial clinical sites now activated, and first-in-human dosing for the Phase 1 study expected in the fourth quarter of 2024.

“We are very excited to provide several significant, positive updates across our rapidly advancing clinical pipeline since our last R&D event in April,” said Peter Blume-Jensen, M.D., Ph.D., chief executive officer, president, and founder of Acrivon. “First, at ESMO earlier today, we presented an updated interim efficacy and safety data cut of our registrational intent ACR-368 Phase 2 study, which showed a confirmed ORR of 62.5% in endometrial cancer patients. Notably, endometrial cancer is a tumor type that we predicted to be sensitive to single agent ACR-368 with our AP3 indication finding screening approach which we have now confirmed in the clinic. The maturing data is particularly encouraging as the lower bound of the 95% confidence interval is now 30%, above our targeted goal for this metric. Moreover, while median duration of response has not yet been reached, it is now approximately 6 months with all responding patients on therapy at time of data cut-off. Given the strength of the data we believe endometrial cancer might provide the first potential approval opportunity for ACR-368. We are actively evaluating potential confirmatory trial designs, including front line, for a potential future label expansion. We are also excited to disclose that the FDA has cleared the IND for our second clinical program, ACR-2316, well ahead of original timeline projections. Clinical trial sites have been activated and are now actively screening patients for enrollment into a Phase 1 study. Today’s update further strengthens the validation of our prospective OncoSignature patient selection method and of our differentiated AP3 platform delivering actionable data across discovery and development.”

ACR-368 Updates and Highlights

- Presented data at ESMO from the ongoing, registrational-intent, multicenter Phase 2 trial of ACR-368 in patients with high grade endometrial cancer. Importantly, all patients enrolled must have progressed on prior anti-PD-1 therapy, unless ineligible. The data were based on 35 safety-evaluable subjects, of which 23 (8 BM+ and 15 BM-) were efficacy-evaluable with at least one on-treatment scan (data cut off July 25, 2024).
  - Reported a confirmed ORR (RECIST 1.1) of 62.5% (95% CI, 30.4-86.5) observed in the cohort of prospectively-selected OncoSignature-positive (BM+) patients who were efficacy-evaluable. Endometrial cancer is a tumor type that was predicted to be sensitive to ACR-368 by AP3-enabled indication screening before any clinical data was generated.
    - Median duration of response (mDOR) was not yet reached (~6 months at time of data cut-off); all responding patients still on therapy
    - Best overall response (BOR) in last prior line predominantly progressive disease (PD) in confirmed ACR-368

responders

- Confirmed responses were observed across molecular and histological subtypes

- Demonstrated the ability of the AP3-based ACR-368 OncoSignature assay to prospectively predict patients sensitive to ACR-368 monotherapy based on updated data that showed a clear segregation of responders in the BM+ versus OncoSignature-negative (BM-) arms (*p-value* = 0.009)
- Observed further evidence of sensitization to ACR-368 by ultra-low dose gemcitabine (ULDG) in a proportion of BM- subjects, with an initial disease control in 8 out of 15 subjects, including 1 confirmed complete response (CR)
- Consistent with past trials and earlier reported data from this trial, the ACR-368 treatment-related adverse events observed were limited, predominantly transient, reversible, mechanism-based hematological AEs, which typically occurred during the first 1-2 cycles of therapy. There was a notable absence of long-lasting myelosuppression, or the typical more severe non-hematological AEs commonly seen with ADCs and chemotherapy.

- Company conducted a blinded third-party KOL market research study which showed strong interest in the emerging clinical profile of ACR-368 (product name blinded) as an important potential therapy in the rapidly evolving treatment landscape of endometrial cancer where second line options are now limited due to anti-PD-1 and chemotherapy having been approved in front line therapy
  - An estimated ~30K new cases of high-grade, locally advanced or metastatic, recurrent (progressed on anti-PD-1 and chemotherapy) endometrial cancer per year
  - ~90% of these patients will progress to second line
  - The recent approval of pembrolizumab plus chemotherapy as a first-line treatment leaves a significant unmet need in the second-line, where the bar from reported chemotherapy efficacy in second-line is an ORR of 14.7% and mPFS of 3.8 months (*Makker et al; N Engl J Medicine, 2022*)
- The ESMO poster presentation is available on Acrivon's website in the "Science and Publications" section

ACR-2316 Updates

- The company today disclosed that the FDA has cleared the IND for its novel, dual WEE1/PKMYT1 inhibitor ACR-2316, ahead of projected timelines
- Multiple clinical sites have been activated for the Phase 1 dose optimization study
- Initial patient dosing expected in fourth quarter 2024 in selected tumor types

AP3 Interactome Updates

- Proprietary, computational analytics platform leveraging machine learning now further advanced for integrated comprehensive analyses across all large, in-house AP3 phosphoproteomic drug profiling data sets.
- Integration enables quantitative analyses to generate actionable insights for rational drug design, predictive biomarkers, resistance mechanisms, and indication finding to be implemented in the clinic
- AP3 Interactome has been deployed to enable indication finding and patient responder identification for ACR-368 and to generate the novel dual WEE1/PKMYT1 inhibitor ACR-2316

Company Webcast and KOL Participation

The company will host a webcast today, Saturday, September 14 at 9:00 a.m. ET to further discuss these data and pipeline updates. A link to the webcast can be found on the investors page of www.acrivon.com.

In addition to company executives, Ramez N. Eskander, M.D., assistant professor of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Diego, CA, a key opinion leader in endometrial cancer will participate in the webcast. Dr. Eskander is the lead author on the influential paper "Pembrolizumab plus Chemotherapy in Advanced Endometrial Cancer" (*N Engl J Med (2023) 388(23):2159-2170*).

About Acrivon Therapeutics
Acrivon is a clinical stage biopharmaceutical company developing precision oncology medicines that it matches to patients whose tumors are predicted to be sensitive to each specific medicine by utilizing Acrivon's proprietary proteomics-based patient responder identification platform, Acrivon Predictive Precision Proteomics, or AP3. The AP3 platform is engineered to measure compound-specific effects on the entire tumor cell protein signaling network and drug-induced resistance mechanisms in an unbiased manner. These distinctive capabilities enable AP3's direct application for

drug design optimization for monotherapy activity, the identification of rational drug combinations, and the creation of drug-specific proprietary OncoSignature companion diagnostics that are used to identify the patients most likely to benefit from Acrivon's drug candidates. Acrivon is currently advancing its lead candidate, ACR-368 (also known as prexasertib), a selective small molecule inhibitor targeting CHK1 and CHK2 in a potentially registrational Phase 2 trial across multiple tumor types. The company has received Fast Track designation from the Food and Drug Administration, or FDA, for the investigation of ACR-368 as monotherapy based on OncoSignature-predicted sensitivity in patients with platinum-resistant ovarian or endometrial cancer. Acrivon's ACR-368 OncoSignature test, which has not yet obtained regulatory approval, has been extensively evaluated in preclinical studies, including in two separate, blinded, prospectively-designed studies on pretreatment tumor biopsies collected from past third-party Phase 2 trials in patients with ovarian cancer treated with ACR-368.

The FDA has granted Breakthrough Device designation for the ACR-368 OncoSignature assay for the identification of ovarian cancer patients who may benefit from ACR-368 treatment. In addition to ACR-368, Acrivon is also leveraging its proprietary AP3 precision medicine platform for developing its co-crystallography-driven, internally-discovered pipeline programs. These include ACR-2316, the company's second clinical stage asset, a potent, selective WEE1/PKMYT1 inhibitor designed for superior single-agent activity as demonstrated in preclinical studies against benchmark inhibitors. The company is also progressing internally- developed preclinical programs, including a cell cycle program with an undisclosed target.

Forward-Looking Statements
This press release includes certain disclosures that contain "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this press release, including statements regarding our future results of operations or financial condition, preclinical and clinical results, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements because they contain words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," or "would" or the negative of these words or other similar terms or expressions. Forward-looking statements are based on Acrivon's current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, risks and uncertainties that are described more fully in the section titled "Risk Factors" in our reports filed with the Securities and Exchange Commission. Forward-looking statements contained in this press release are made as of this date, and Acrivon undertakes no duty to update such information except as required under applicable law.

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