Acrivon Therapeutics to Reveal the Molecular Mechanisms Driving Strong Single-Agent Activity of ACR-2316, its AP3-Enabled Clinical Stage WEE1/PKMYT1 Inhibitor, at the AACR Annual Meeting 2025

April 25, 2025

Presentation to highlight how AP3 Generative Phosphoproteomic analyses uncover how ACR-2316 induces mitotic and replicative tumor cell death, and the mechanisms underlying its superior potency observed preclinically

Phase 1 trial of ACR-2316 ahead of schedule with three dose-escalation cohorts completed; solid tumor shrinkage already observed at dose level three, well below the projected recommended Phase 2 dose

WATERTOWN, Mass., April 25, 2025 (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, announced it will present data from AP3 Generative Phosphoproteomic analyses of ACR-2316-regulated CDK1-, CDK2-, and PLK1-induced pathways at the American Association for Cancer Research (AACR) Annual Meeting taking place April 25-30, 2025 in Chicago.

ACR-2316 is a selective WEE1/PKMYT1 inhibitor, which has shown differentiated and superior anti-cancer activity in preclinical studies against clinical benchmark inhibitors and is currently in an ongoing Phase 1 monotherapy clinical study. Using AP3-based Indication Finding and AP3-based analyses of in-house and publicly available data, the company is enrolling patients in the clinical trial with certain high unmet need solid tumor types selected based on predicted sensitive to ACR-2316. Dose levels (DLs) 1, 2 and 3 have been cleared without safety concerns or dose-limiting toxicities (DLTs) by the safety review committee, and DL4 is now enrolling. Drug target engagement was observed already at DLs 1 and 2 using the company’s clinical mass-spectrometry-based AP3 profiling, with evidence of approximate dose proportionality based on plasma pharmacokinetic analyses. Notably, initial clinical activity of ~25% RECIST tumor shrinkage and reduction of metastatic lesions throughout the chest, abdomen and pelvis was already observed at DL3.

“ACR-2316 was rationally designed through AP3-based SAR to induce desirable anti-tumor pathway effects inside a cell and to overcome the limitations of single-target WEE1 and PKMYT1 inhibitors. Our Phase 1 study of ACR-2316 is advancing rapidly, and we are excited about these encouraging observations, including early clinical activity,” said Peter Blume-Jensen, M.D., Ph.D., chief executive officer, president, and founder of Acrivon Therapeutics. “Uniquely enabled by our Generative Phosphoproteomics AP3 platform, ACR-2316 is optimized to achieve superior single-agent activity, complete tumor regression and pro-apoptotic tumor cell death with a favorable therapeutic index, as demonstrated in preclinical studies. At AACR, we look forward to sharing exciting data which show how signaling pathways acted upon by ACR-2316 mechanistically deliver potent activity.”

Poster Details:

Poster Title:	Detailed mechanistic understanding of ACR-2316, a novel, clinical-stage WEE1/PKMYT1 inhibitor, rationally designed for superior single-agent activity through potent activation of CDK1, CDK2, and PLK1 using Acrivon’s Generative Phosphoproteomics AP3 platform
Abstract Number:	357
Poster Section / No:	17 / 1
Session Category:	Experimental and Molecular Therapeutics
Session Title:	Cell Cycle Effects of Anticancer Drugs
Presenter:	Lei Shi, Ph.D.
Date and Time:	Sunday, April 27 | 2:00-5:00 p.m. CT

About Acrivon Therapeutics
Acrivon is a clinical stage biopharmaceutical company discovering and developing precision oncology medicines for patients whose tumors are predicted to be sensitive to each specific medicine by utilizing its proprietary Generative Phosphoproteomics 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 yielding terabytes of high resolution proprietary quantitative data for pathway-based drug design, indication finding, and response prediction. These distinctive capabilities enable AP3’s direct application for streamlined rational drug discovery 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, focusing on endometrial cancer. 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 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 designations for the ACR-368 OncoSignature assay for the identification of patients with endometrial cancer 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 novel, potent, selective WEE1/PKMYT1 inhibitor designed for superior single-agent activity through strong activation of not only CDK1 and CDK2, but also of PLK1 to drive pro-apoptotic cell death, as demonstrated in preclinical studies against benchmark inhibitors. In addition, the company has a preclinical cell cycle program with an undisclosed target.

Acrivon has developed its AP3 Interactome, a proprietary, computational analytics platform driven by Generative Phosphoproteomics machine learning for integrated comprehensive analyses across all large, in-house AP3 phosphoproteomic drug profiling data sets to advance its in-house research programs.

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.

Investor and Media Contacts:
Adam D. Levy, Ph.D., M.B.A.
alevy@acrivon.com

Alexandra Santos
asantos@wheelhouselsa.com