UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 14, 2024

Acrivon Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-41551**	**82-5125532**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

480 Arsenal Way, Suite 100 **Watertown, Massachusetts** **(Address of Principal Executive Offices)**	**02472** **(Zip Code)**

(617) 207-8979
(Registrant's Telephone Number, Including Area Code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value	ACRV	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure

On September 14, 2024, Acrivon Therapeutics, Inc. (the "Company") issued a press release reporting Phase 2 clinical data ofACR-368 in patients with endometrial cancer that the Company presented at the European Society of Medical Oncology (ESMO) Congress 2024 in Barcelona, Spain on September 14, 2024. The press release also announced that the Investigational New Drug 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. The press release also provided progress updates on the Company's AP3 Interactome, the Company's proprietary, computational analytics platform.

On September 14, 2024, the Company hosted a virtual corporate R&D event, where the Company reviewed theACR-368 clinical data, ACR-2316 updates, and the progress on the Company's AP3 Interactome platform. The Company also reiterated previous guidance that the Company expects that its existing cash, cash equivalents and investments of $220.4 million as of June 30, 2024, will be sufficient to fund its operating expenses and capital expenditure requirements into the second half of 2026. Copies of the press release and the presentation from the corporate R&D event are attached hereto as Exhibits 99.1 and 99.2 and incorporated by reference into this Item 7.01 of this Current Report on Form 8-K.

The information set forth under Item 7.01 of this Current Report on Form8-K, including Exhibits 99.1 and 99.2, is being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section and shall not be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 8.01 Other Events

ACR-368 Phase 2 Clinical Data

On September 14, 2024, the Company presented clinical data at ESMO Congress 2024 from its ongoing registrational intent, multicenter Phase 2 trial of ACR-368 in patients with locally advanced or metastatic, recurrent endometrial cancer. The data were based on 35 safety-evaluable subjects, of which 23 (8 OncoSignature-positive and 15 OncoSignature-negative) were efficacy-evaluable with at least one on-treatment scan. The data presented was based on data available from the trial's electronic data capture system as of July 25, 2024.

A confirmed objective response rate ("ORR") (RECIST 1.1) of 62.5% (95% CI,30.4-86.5) was observed in the cohort of prospectively-selected OncoSignature-positive patients who were efficacy-evaluable and who had all progressed on prior anti-PD-1 therapy. All confirmed responders continued to be on treatment and median duration of response had not yet been reached (~6 months at time of data cut-off).

Best overall response in last prior line predominantly progressive disease in confirmedACR-368 responders.

The data further validated the Company's AP3-based ACR-368 OncoSignature assay, which is used for prospective patient selection in this registrational intent trial, achieving a clear segregation of responders in the OncoSignature-positive versus OncoSignature-negative arms (p-*value* = 0.009).

Further evidence of sensitization to ACR-368 by ultra-low dose gemcitabine in a proportion of OncoSignature-negative subjects was observed, with an initial disease control in 8 out of 15 subjects, including 1 confirmed complete response.

Consistent with past trials and earlier reported data, theACR-368 treatment-related adverse events were limited, predominantly transient, reversible, mechanism-based hematological adverse events, 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 adverse events commonly seen with antibody-drug conjugates and chemotherapy.

ACR-2316 Updates

The Company also announced that the Investigational New Drug application for its next clinical candidate,ACR-2316, has been cleared by the FDA with initial clinical sites now activated ahead of schedule, and first-in-human dosing for the Phase 1 study now expected in the fourth quarter of 2024.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits:

Exhibit Number	Exhibit Description
99.1	Press Release, dated September 14, 2024
99.2	Acrivon Therapeutics, Inc. Presentation, dated September 14, 2024
104	Cover Page Interactive Data File (formatted as Inline XBRL).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Acrivon Therapeutics, Inc.

Dated: September 16, 2024

By: /s/ Peter Blume-Jensen
Name: Peter Blume-Jensen, M.D., Ph.D.
Title: Chief Executive Officer and President

Exhibit 99.1

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

- *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, Massachusetts, September 14, 2024 – 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 theACR-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 includeACR-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.

Investor and Media Contacts:

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Exhibit 99.2

Acrivon Therapeutics

ACRIVON PREDICTIVE PRECISION PROTEOMICS (AP3)

OVERCOMING LIMITATIONS OF GENETICS-BASED PRECISION MEDICINE

CORPORATE R&D EVENT

SEPTEMBER 14, 2024

FORWARD-LOOKING STATEMENTS

Certain information contained in this presentation includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations. 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. Our forward-looking statements are based primarily on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and results of operations. The outcome of the events described in the forward-looking statements is subject to risks and uncertainties, including the factors described in our filings with the U.S. Securities and Exchange Commission. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this presentation. The results, events, and circumstances reflected in the forward-looking statements may not be achieved or occur, and actual results, events, or circumstances could differ materially from those described in the forward-looking statements.

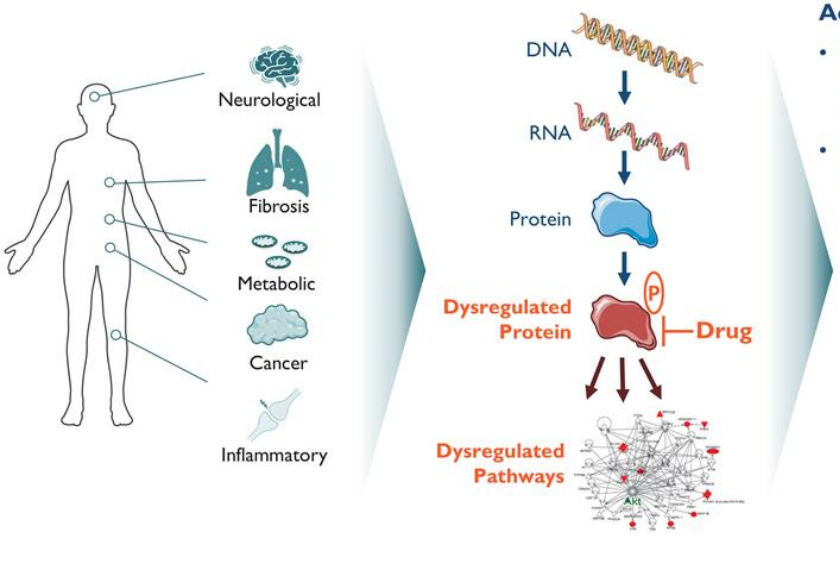
You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this presentation. We undertake no obligation to update any forward-looking statements or to reflect new information or the occurrence of unanticipated events, except as required by law.

OUTLINE

- Acrivon Therapeutics and AP3 overview
- Data update on the prospective ACR-368 registrational intent Phase 2 trial in endometrial cancer
- Update on ACR-2316, an AP3-derived dual WEE1/PKMYT1 inhibitor cleared for Phase 1
- Intro to AP3 Interactome v.2: Real-time actionable analyses of Acrivon proprietary AP3 data
- Live Q&A

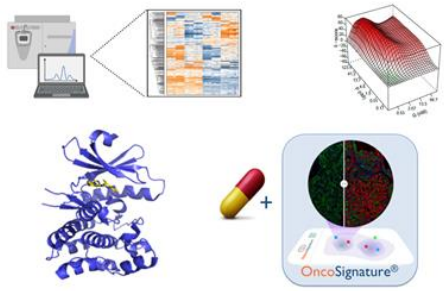
For a comprehensive corporate deck, please visit: https://Acrivon.com

ACRIVON THERAPEUTICS – A NEXT-GENERATION PRECISION MEDICINE COMPANY



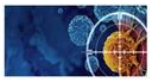
Acrivon Predictive Precision Proteomics (AP3)

- Enables an exact match between the disease-driving, dysregulated pathways with a drug's mechanism of action (Acrivon meaning ≈ exact, accurate)
- Broadly applicable in R&D (biological SAR, resistance, patient responders); leveraged for internal pipeline



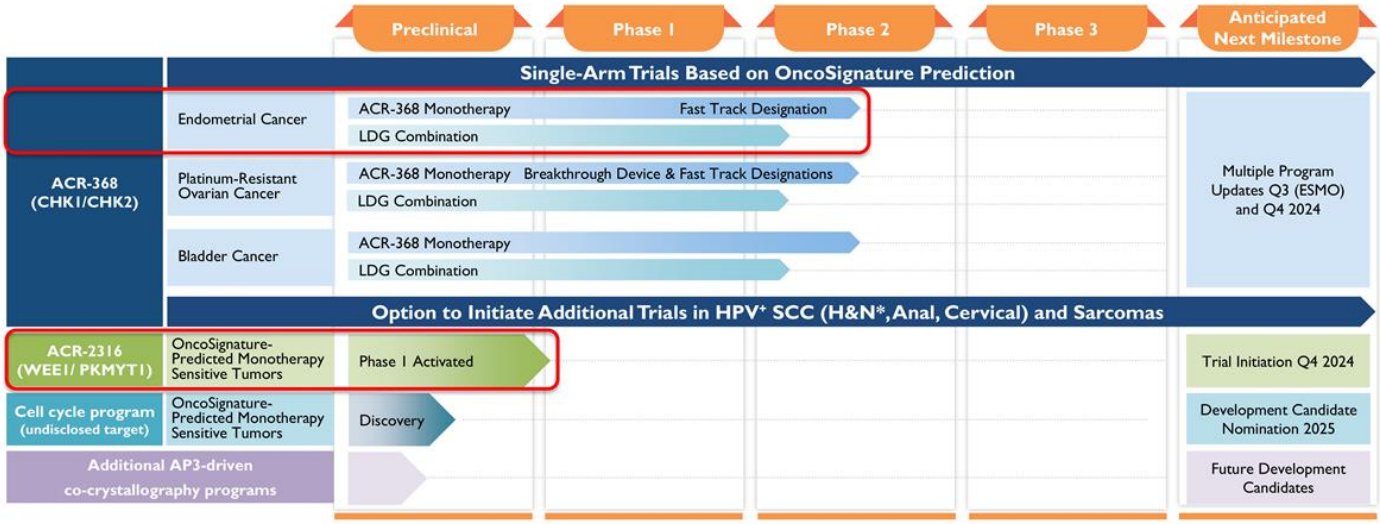
Blume-Jensen, P & Hunter, T: Oncogenic kinase signaling *Nature* (2001)
Olsen, JV et al: Global, in vivo, and site-specific phosphorylation dynamics in signaling networks *Cell* (2006);
Andersen, JN et al: Pathway-based identification of biomarkers for targeted therapeutics: personalized oncology with PI3K pathway inhibitors *Sci Transl Med* (2010)

AP3 DEVELOPED TO OVERCOME CRITICAL CHALLENGES FACING BIOPHARMA INDUSTRY

	Challenge	Acrivon Predictive Precision Proteomics (AP3)
	Discovering **potent** compounds suitable for **clinical monotherapy**	Optimal target/pathway selectivity for rapid generation of single agent active compounds
	Determining **which patients will benefit from** those drugs	Identification of drug-sensitive indications and patients for actionable precision medicine
	Preventing or reducing resistance to **maximize response durability**	Ability to rapidly identify and overcome resistance mechanisms

AP3 is a proprietary, machine learning-enabled internal R&D engine that effectively addresses these challenges, driving rapid advancement of our pipeline

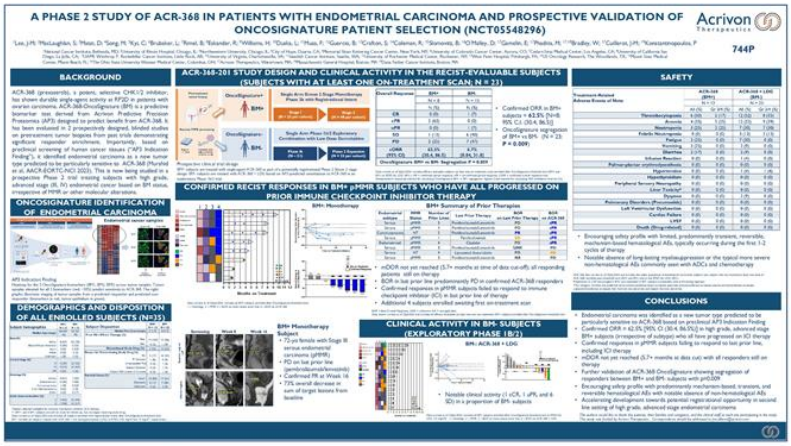
ACRIVON PIPELINE



ACR-368 Monotherapy	Registrational intent Phase 2 single arm trials based on predicted sensitivity to ACR-368 monotherapy in OncoSignature-positive patients
LDG Combination	Exploratory Phase 1b/2 single arm trials of ACR-368 in combination with low dose gemcitabine, or LDG, in OncoSignature-negative patients

*Investigator-Initiated Trial (IIT) activated at Moffitt Cancer Center

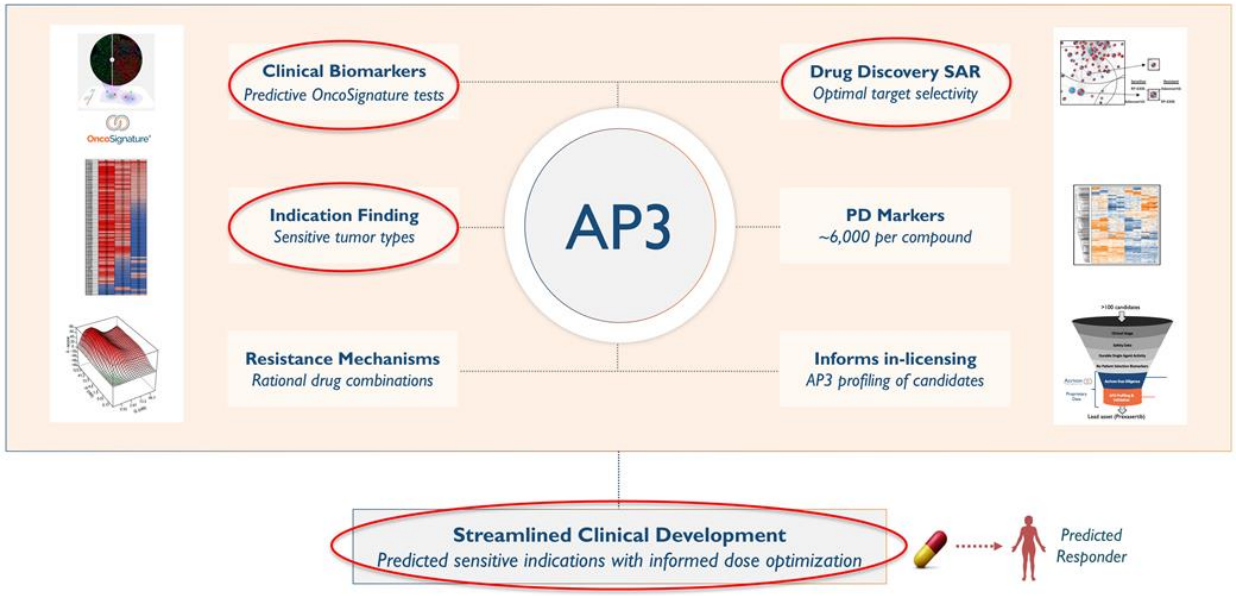
ESMO 2024: Interim data from the registrational intent Phase 2 prospective clinical trial in endometrial cancer



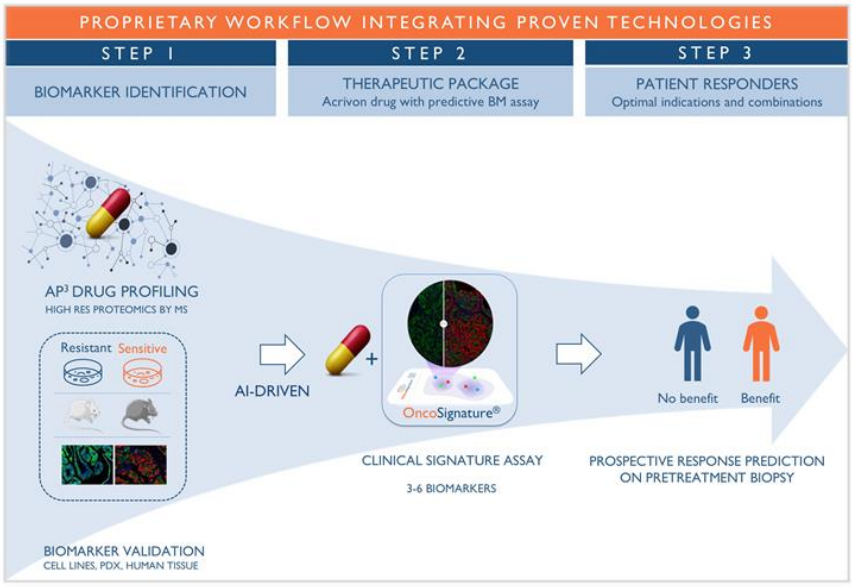
Data cut as of July 25, 2024

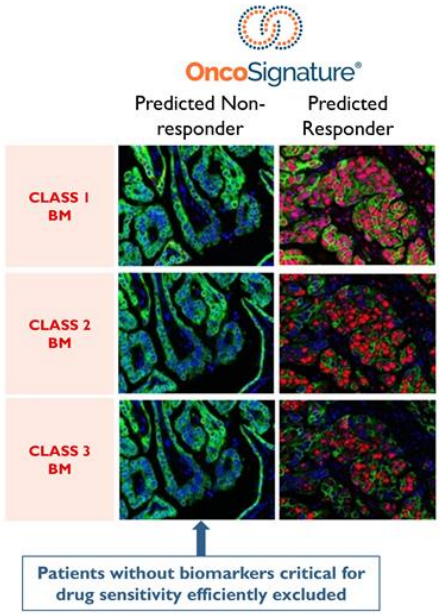
Poster available on Acrivon's website: https://acrivon.com/science/#publications-posters

AP3-BASED DRUG DISCOVERY AND CLINICAL DEVELOPMENT IN PREDICTED SENSITIVE SUBJECTS AND TUMOR TYPES



AP3 PLATFORM: DRUG RESPONSE PREDICTION IN INDIVIDUAL PATIENTS

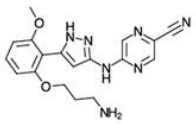




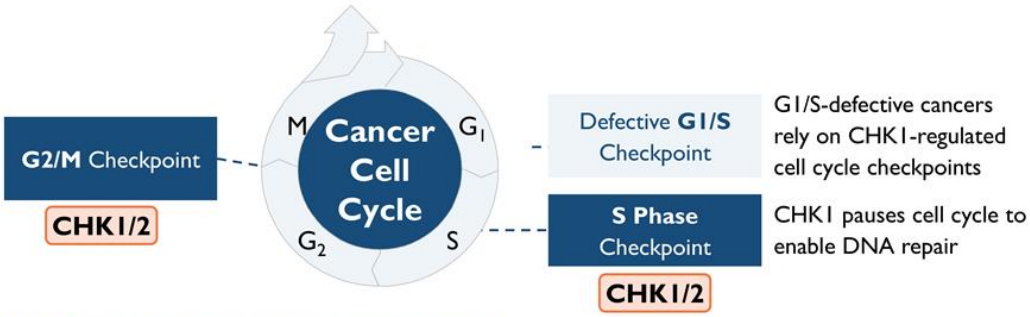
"Disease Pathway-Based Method to Generate Biomarker Panels Tailored to Specific Therapeutics for Individualized Treatments": EP 2 229 589, issued June 10, 2015; US2017/0067877A9, pending. OncoSignature® *is a Registered Trademark: US Reg. No. 5,718,472; Int. Cl. 5, 42. Intl. Reg. 1382289*

ACR-368: A CLINICALLY ACTIVE PHASE 2 CHK1/2 INHIBITOR

- ATP-competitive inhibitor of CHK1 (0.9 nM) and CHK2 (8 nM)
- Exclusively in-licensed from Eli Lilly & Company (WW rights); originally discovered by Array (Pfizer)
- CoM patent exp. Oct., 2030; Salt-form exp. Apr., 2037
- Balanced inhibition of both CHK1 and CHK2 believed important for RECIST monotherapy activity



ACR-368 (MW): 365.4

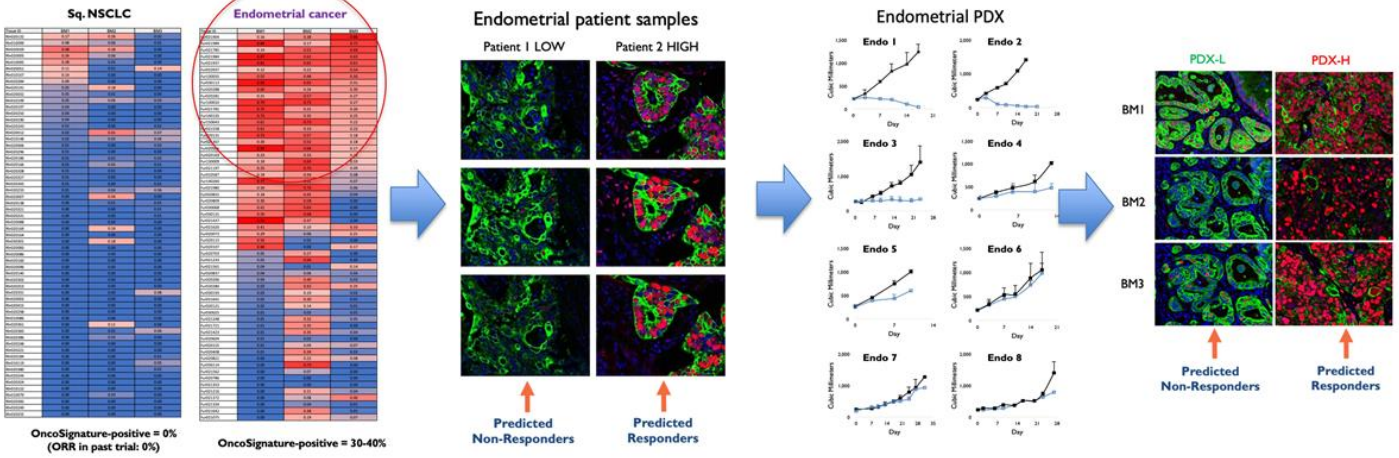


DRUG TARGET PROFILE AT TIME OF IN-LICENSING

- **Durable monotherapy activity:** Platinum-resistant ovarian and squamous cell cancers (Anal and H&N)
- **Large safety database, favorable safety profile:** >1,000 patients treated (~50% mono, ~50% in combination)
- **Ideal for AP3 method:** Proven clinical activity, but requires patient responder identification to achieve sufficient ORR

ENDOMETRIAL CANCER IS AN AP3-PREDICTED ACR-368-SENSITIVE TUMOR

ACR-368 OncoSignature-based indication finding prior to trial entry → ACR-368 OncoSignature imaging demonstrates addiction to CHK1/2 DDR axis → Confirmation of predicted sensitivity in genetically non-modified PDX models → Confirmation of ACR-368 OncoSignature prediction in PDX tumor tissues pretreatment



in >1,000 cancer patients treated with ACR-368 in Lilly-sponsored trials, endometrial cancer was not tested

HIGH GRADE ADVANCED STAGE ENDOMETRIAL CANCER
OPPORTUNITY HAS OPENED FOR ≥ 2ND LINE (POST ANTI-PD-1)

ACR-368 Target Indication:

- High grade, locally advanced or metastatic, recurrent endometrial cancer
- Significant unmet need, attractive commercial potential
- Must have recurred after prior chemo and PD-1/PD-L1 inhibitor therapy[1]
- Irrespective of molecular (MMR, p53, other) alterations and subtype (serous, endometrioid, clear cell, carcinosarcoma)

SOC:

- ≥2nd line (post-PD-1 + chemo) ~14.7% ORR, mPFS 3.8 months[2]
- ≥3rd line ~9% ORR, mPFS 2.8 months[3]

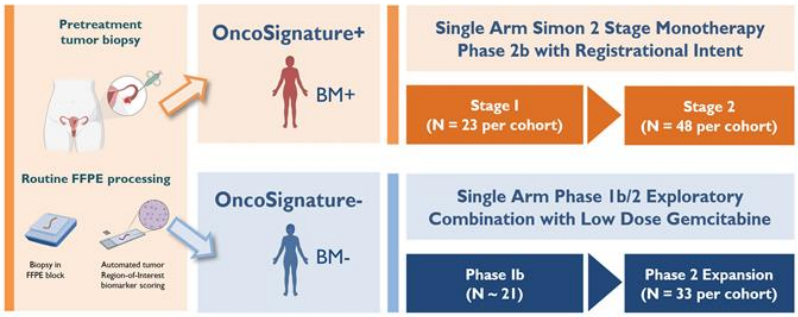
ACR-368 Target Product Profile:

- ≥25% ORR with CI lower bound >20%; mDoR ≥5.5 months

[1]Unless ineligible for PD-1/PD-L1 therapy
[2]Eskander R et al, NEJM, 2023; Mirza MR et al, NEJM, 2023; Makker V et al, NEJM, 2022
[3]Ray-Coquard I et al, BJC, 2013

ACR-368-201 TRIAL AND ENROLLMENT IN ENDOMETRIAL CANCER

ACR-368-201 Trial



https://clinicaltrials.gov/study/NCT05548296

Enrollment in Endometrial Cancer

	April 2024 Corporate R&D Event[1]			ESMO 2024[2]		
Endometrial Cancer	BM+	BM-	Total	BM+	BM-	Total
Safety-Evaluable (enrolled ≥1 dose)	7	11	18	12	23	35
Efficacy-Evaluable (≥1 on-treatment scan)	5	5	10	8	15	23
BM+% (enrolled BM+/Total)	38.9%			34.3%		

[1]https://ir.acrivon.com/news-events/events-presentations
[2]https://acrivon.com/science/#publications-posters

Ongoing enrollment in ovarian and bladder cancer cohorts with update planned for future date

DEMOGRAPHICS AND SUBJECT DISPOSITION (N=35)

Subject Demographics	BM+ N = 12	BM- N = 23
Median Age (range)	66 (60-76)	68 (42-78)
Race (%)		
White	8 (67)	16 (70)
Black/African American	3 (25)	3 (13)
Asian	0 (0)	3 (13)
Other	0 (0)	1 (4)
Unknown	1 (8)	0 (0)
Current Stage (%)		
III	3 (25)	12 (52)
IV	9 (75)	10 (43)
unk	0 (0)	1 (4)
Histology (%)		
Serous	8 (67)	7 (30)
Endometrioid	3 (25)	7 (30)
Carcinosarcoma	1 (8)	3 (13)
Clear Cell Carcinoma	0 (0)	2 (9)
Other	0 (0)	4 (17)
ECOG Status at Baseline (%)		
0	5 (42)	10 (43)
1	7 (58)	13 (57)

Subject Disposition	BM+ N = 12	BM- N = 23
Median Prior Lines (range)	2 (1-4)	3 (1-4)
Prior PD-1/PD-L1 Therapy (%)		
Yes	12 (100)	22 (96)
No	0 (0)	1 (4)*
Discontinued Study Drug (%)	3 (25)	13 (57)
Reason for Discontinuing Study Drug (%)		
PD	2 (17)	10 (43)
PI Decision	1 (8)	0 (0)
Unacceptable Tox	0 (0)	1 (4)
Subject Decision	0 (0)	1 (4)
Subject Withdrawal of Consent	0 (0)	1 (4)
Survival Status (%)		
Alive^	10 (83)	14 (61)
Deceased	2 (17)	7 (30)
Unknown	0 (0)	2 (9)

*Subject deemed ineligible for anti-PD-1 therapy.
^1 BM+ and 4 BM- subjects are still on study for follow-up, but no longer receiving study drug.
Data current as of 25July2024 and includes all subjects enrolled with registrational intent
BM- includes all subjects treated with ACR-368 + low dose gemcitabine (LDG) at RP2D (105 mg/m^2 and 10 mg/m^2, respectively).

SIGNIFICANT ACR-368 RESPONDER ENRICHMENT IN EFFICACY-EVALUABLE SUBJECTS[1] (N=23) IN REGISTRATIONAL INTENT PHASE 2 TRIAL

Meaningful positive data maturation since April R&D Event[2]

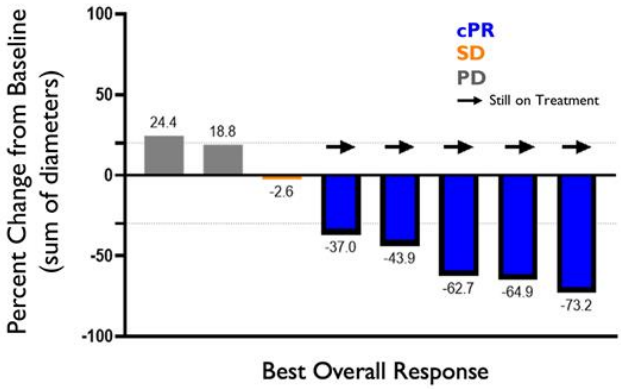
- **Prospective initial validation of the AP3-based ACR-368 OncoSignature now achieved for endometrial cancer (P = 0.009** vs P = 0.083)
- **Confirmed ORR in BM+ subjects now 62.5% with the lower bound of 95% C.I. 30.4%** (vs. 22.9%)
- **Confirmed ACR-368 responders still on therapy; mDoR not yet reached (~6 months at time of data-cut** vs ~2 months)

Overall Response	BM+ Monotherapy	BM- LDG Combination	Total
	N = 8	N = 15	N=23
	N (%)	N (%)	N (%)
CR	0 (0)	1 (7)	1 (4)
cPR	5 (63)	0 (0)	5 (22)
uPR	0 (0)	1 (7)	1 (4)
SD	1 (13)	6 (40)	7 (30)
PD	2 (25)	7 (47)	9 (39)
cORR (95% CI)	**62.5% (30.4, 86.5)**	**6.7% (0.84, 31.8)**	**26% (12.3,46.8)**
OncoSignature BM+ vs BM- Segregation P = 0.009			

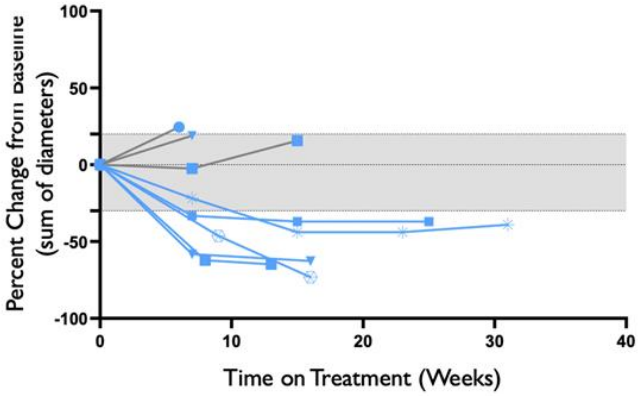
[1]Subjects with ≥1 on-treatment scan
[2]https://ir.acrivon.com/news-events/events-presentations

CLINICAL ACTIVITY IN BM+ PATIENTS WHO HAVE ALL PROGRESSED ON PRIOR ANTI-PD-1 THERAPY

Confirmed ORR = 62.5%
95% C.I. (30.4%, 86.5%)

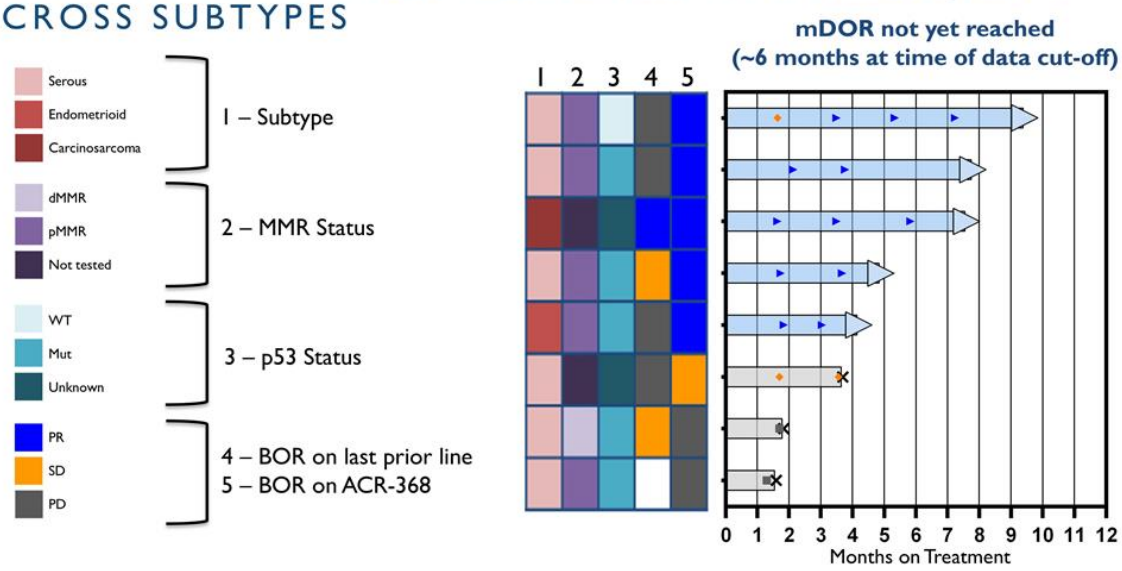


Significant disease control (75%) with most RECIST responses occurring early



Data current as of 25July2024, includes all BM+ subjects

ONGOING CONFIRMED RESPONSES IN BM+ SUBJECTS ACROSS SUBTYPES



- Durable responses in patients who all progressed on prior anti-PD-1 and whose BOR in last prior line was mostly PD
- Most patients are pMMR and p53 mutant, consistent with their prevalence in high grade endometrial cancer
- ACR-368 OncoSignature prediction is independent of molecular (incl. MMR) and histological subtype

Data current as of 25July2024

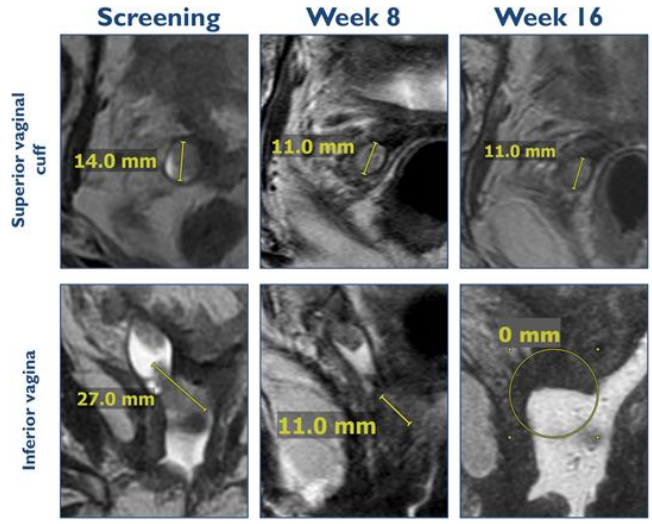
CONFIRMED RESPONSES IN SUBJECTS WHO ALL PROGRESSED ON PRIOR ANTI-PD-1

Endometrial subtype	# Prior Lines	Last Prior Therapy (LPT)	BOR on LPT	BOR on ACR-368
Serous	3	Pembrolizumab/Lenvatinib	PD	cPR
Serous	2	Pembrolizumab/Lenvatinib	PD	cPR
Endometrioid	4	Cisplatin	PD	cPR
Serous	1	Pembrolizumab	SD	cPR
Carcinosarcoma	2	Pembrolizumab/Lenvatinib	PR	cPR
Serous	4	Liposomal doxorubicin	PD	SD
Serous	3	Pembrolizumab/Lenvatinib	*UNK*	PD
Serous	3	Pembrolizumab/Lenvatinib	*NA*	PD

- All confirmed responders progressed on prior PD-1 therapy and majority had BOR = PD on last prior line of therapy
- Only 1 RECIST response amongst 6 patients with BOR data from LPT

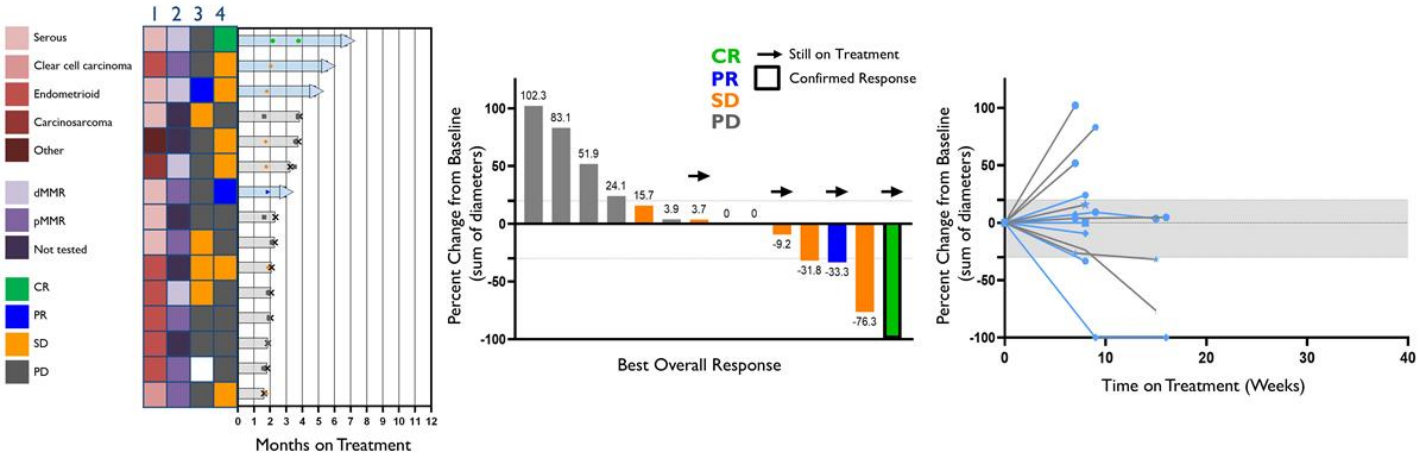
BOR = Best Overall Response, UNK = unknown, NA = not applicable, NT = not tested
Data shown current as of 25Jul2024 and includes all efficacy-evaluable (at least one scan on-treatment) BM+ subjects

DEEP, RAPID RESPONSES SEEN IN PATIENTS WITH LARGE TUMOR LESIONS



- 72-yo female with Stage III serous endometrial carcinoma (pMMR)
- PD on last prior line (pembrolizumab/lenvatinib)
- Confirmed PR at Week 16
- 73% overall decrease in sum of target lesions from baseline

EVIDENCE OF LDG SENSITIZATION IN PROPORTION OF BM- SUBJECTS IN EXPLORATORY PHASE 1B/2 TRIAL



- Initial disease control (1 cCR, 1 uPR, and 6 SD) observed in a proportion of BM- subjects
- LDG sensitization may potentially increase ORR across BM+ and BM- patients

Data current as of 25July2024, includes all BM- subjects enrolled at RP2D for LDG (10 mg/m²).
1– Histology; 2 – MMR; 3 – BOR on most recent prior line; 4 – BOR on ACR-368 + LDG

ENCOURAGING SAFETY PROFILE

- **Limited, predominantly transient, reversible, mechanism-based hematological AEs, which typically occurred during the first 1-2 cycles of therapy**
- **Notable absence of long-lasting myelosuppression or the typical more severe non-hematological AEs commonly seen with ADCs and chemotherapy**

Treatment-Related Adverse Events of Note	ACR-368 (BM+) N = 12		ACR-368 + LDG (BM-) N = 23	
	All (%)	**Gr 3/4 (%)**	All (%)	**Gr 3/4 (%)**
Thrombocytopenia	6 (50)	**2 (17)**	12 (52)	**8 (35)**
Anemia	4 (33)	**3 (25)**	12 (52)	**9 (39)**
Neutropenia	3 (25)	**3 (25)**	7 (30)	**7 (30)**
Febrile Neutropenia	0	**0**	3 (13)	**3 (13)**
Fatigue	3 (25)	**0**	7 (30)	**0**
Vomiting	3 (25)	**0**	2 (9)	**0**
Diarrhea	2 (17)	**0**	2 (9)	**0**
Infusion Reaction	0	**0**	1 (4)	**0**
Hypertension	0	**0**	1 (4)	**1 (4)**
Dyspnea	0	**0**	2 (9)	**0**

ACR-368 data current as of 25July2024 and includes the safety population of endometrial carcinoma subjects (any subject who has received at least one dose of ACR-368) enrolled (BM+ and BM-) and at the RP2D for LDG (BM-).
Prophylactic G-CSF encouraged in BM+ and mandated in BM- subjects (compatible with q14d dosing regimen).

BLINDED KOL MARKET RESEARCH UNDERSCORES ENDOMETRIAL CANCER REPRESENTS SIGNIFICANT OPPORTUNITY FOR ACR-368

- Endometrial cancer (EC) projected to be the third most prevalent cancer and the fourth leading cause of cancer-related death among women by 2040[1]
  - Incidence = 67,880, prevalence = 865,000 in the US (2023)*; Incidence increasing by 1-3% per year
  - Mortality = 13,250 in the US (2023); 5-year survival ~ 80%*
  - High grade EC accounts for majority of EC deaths each year

- Second line (2L) now represents a high unmet need
  - New cases of high grade, recurrent EC (progressed on anti-PD-1 + chemo) ~30K patients/year
  - 90% of cases believed to progress to 2L therapy
  - Recent front-line approvals of anti-PD-1 plus chemo followed by anti-PD-1 only[1,2] for high grade EC reduces/eliminates pembro + lenvatinib[3] as viable 2L option for most patients
  - Reported chemotherapy efficacy in 2L is ORR = 14.7% and mPFS = 3.8 months[3]

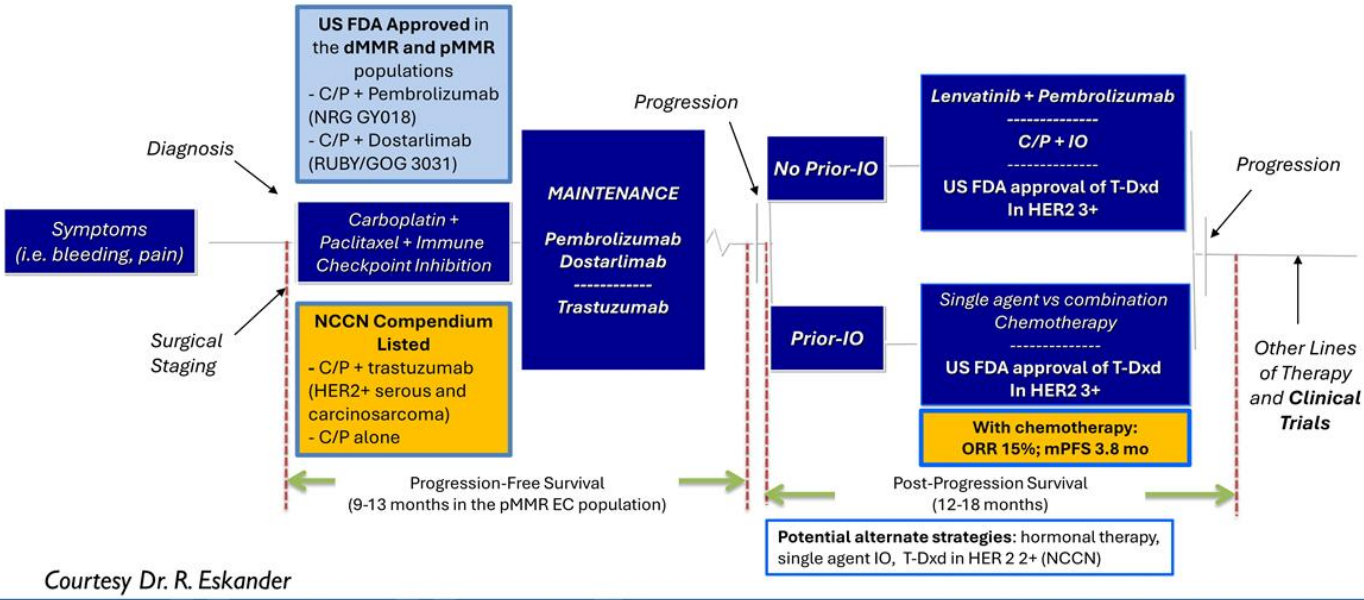
*SEER database
[1]Eskander et al, NEJM 2023; [2]Mirza et al, NEJM 2023; [3]Makker et al, NEJM 2022

BLINDED KOL MARKET RESEARCH SUGGESTS ACR-368 PROFILE ATTRACTIVE TO GYNECOLOGIC ONCOLOGISTS

Themes	Representative quotes	Implications
Huge unmet need still exists in endometrial cancer treatment, especially pMMR	"People that develop recurrence almost invariably do not survive their endometrial cancer." "I believe that in pMMR the contribution of immune therapy is modest." "Those patients (pMMR) we know they don't have as robust as response as those patients that are mismatch repair deficient. Certainly, that's a big unmet need."	**Clinicians eager to embrace new therapeutic options especially in challenging to treat molecular sub-groups**
Significant SOC gap and unmet need exists in 2L opportunity for ACR-368	"That's really where there is the biggest opportunity is – in 2L." "I think everybody's struggling with what to do for 2L therapy." "I would say that you would really want to see something with a response rates north of 30% to really get people excited about that but really the bar is above 20% and would be interesting." "If you had a 20% or 25% response rate, that would be pretty good"	**Recent changes to standard of care leaves opportunity for significant penetration with new 2L therapies**
Biomarker driven approach highly attractive and justified for high ORR	"I know the FDA is very interested in companion diagnostics. I think that they really want to see that the work is being done to understand the responders." "If you could predict which patients would respond so that the patients that you chose would be higher, then I think you'd be in like Flynn." "Over 60% ORR? I hope such a compound really exists!"	**That ACR-368 OncoSignature is independent of genetic background or histology further favorably differentiates the agent**

Source: Single blinded, proprietary third-party market research with endometrial KOLs conducted August-September 2024

EVOLVING TREATMENT LANDSCAPE FOR THE MANAGEMENT OF ADVANCED STAGE OR RECURRENT ENDOMETRIAL CANCER



Courtesy Dr. R. Eskander

DEVELOPMENT PATH FOR ACR-368 IN ENDOMETRIAL CANCER

- Accelerated approval pathway
  - Ongoing single arm registrational intent Phase 2 monotherapy endometrial cancer trial represents the first potential approval opportunity for ACR-368

- Confirmatory trial strategy
  - Evaluating options to potentially move towards new front line setting
    - Randomization anti-PD-1 vs anti-PD-1 + ACR-368 post C/P + anti-PD-1 (sub-group analysis; MMR status in all-comer)*
  - Potential ≥2nd line options:
    - ACR-368 + ULDG in all-comer patients

*Based on current clinical data showing cPRs in patients progressing on prior anti-PD-1 together with a strong rationale for, and preclinical data demonstrating additive/synergistic activity of ACR-368 and anti-PD-1 (Refs: Lyer et al, Cancer Disc 2021; McGrail et al, Sci Transl Med 2021; Sen et al, Cancer Disc 2019)

ACR-368 POTENTIAL IN HIGH UNMET TUMOR TYPES BEYOND ENDOMETRIAL, OVARIAN, AND BLADDER CANCER

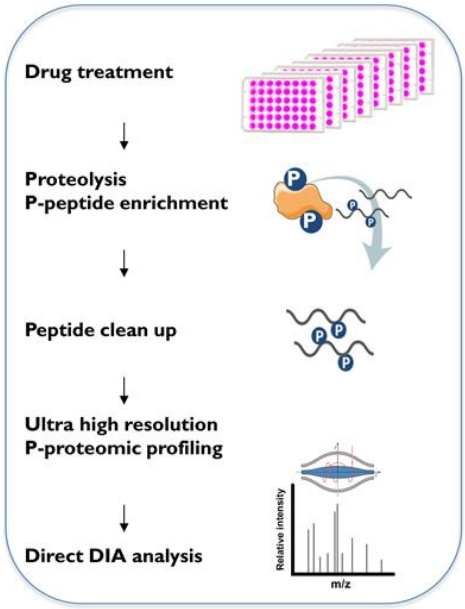
- Enrollment is continuing in our ongoing multicenter phase 2 trials in ovarian and bladder cancer with planned update at a future date
- ACR-368 has also shown promising clinical activity in HPV+ squamous cell cancers (SCC), and sarcomas*
- HPV+ SCC are of increasing incidence (~50,000-60,000 new cases per year in the US) and includes ~70-80% of oropharyngeal H&N, ~20% of esophageal, ~90% of cervical, and 95% of anal cancers**
- SCCHN: Dr. C Chung, MD, Chair, Moffitt Cancer Center has begun an investigator-initiated trial with ACR-368 + ULDG in both HPV+ and HPV- SCCHN post anti-PD-1. IND cleared and site is activated
- **HPV+ SCC represent tumor types of high unmet need and attractive option for next Acrivon-sponsored trial(s) with ACR-368**

*Hong et al, CCR 2018, Slotkin et al, ASCO Annual Meeting 2022
**CDC 2023; ICO/IARC Information Centre on HPV and Cancer 2023; Gribb et al, Dela J Public Health 2023, NCI 2023

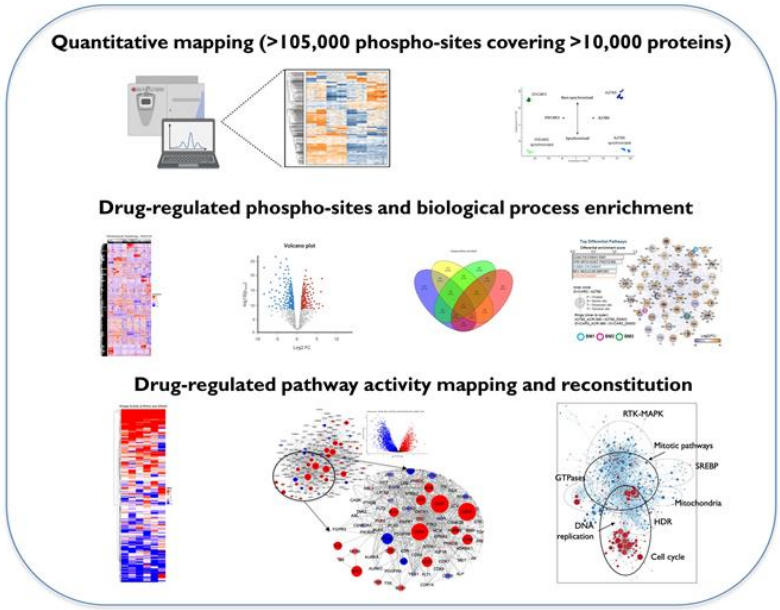
ACR-2316, a potent, novel, dual WEE1/PKMYT1 inhibitor optimized for superior single agent activity and therapeutic index

IND CLEARED AND FIRST CLINICAL SITES ACTIVATED AHEAD OF SCHEDULE

STREAMLINED AP3-BASED DESIGN OF COMPOUNDS FOR SUPERIOR SINGLE AGENT ACTIVITY AND THERAPEUTIC INDEX



High resolution and throughput MS-based P-proteomics



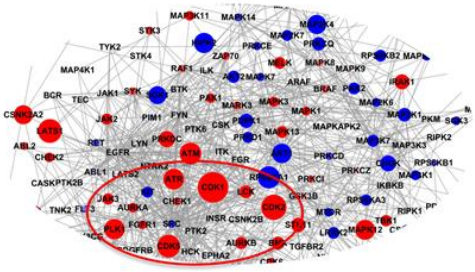
AP3 enables pathway-based drug design for optimal drug properties

ACR-2316: UNIQUELY ENABLED BY AP3 TO OVERCOME LIMITATIONS OF CURRENT WEE1 AND PKMYT1 INHIBITORS

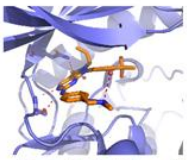
Program goals (superior therapeutic index):

- **Superior single agent activity (AP3)**
  - Potent activation of CDK1, CDK2, and PLK1 and quenching of resistance through balanced WEE1/PKMYT1 inhibition to ensure robust pro-apoptotic tumor death
- **High selectivity for minimal AEs (co-crystallography)**
  - Structure-guided design to limit adverse events (AEs) to be strictly mechanism-based, transient, short-lived
- **Streamlined clinical development (ACR-2316 OncoSignature)**
  - To identify/prioritize sensitive indications prior to clinical start and for drug target engagement-based dose optimization during Phase 1

AP3 used for pathway-based optimization to achieve superior single agent activity



Co-crystallography for drug design and selectivity

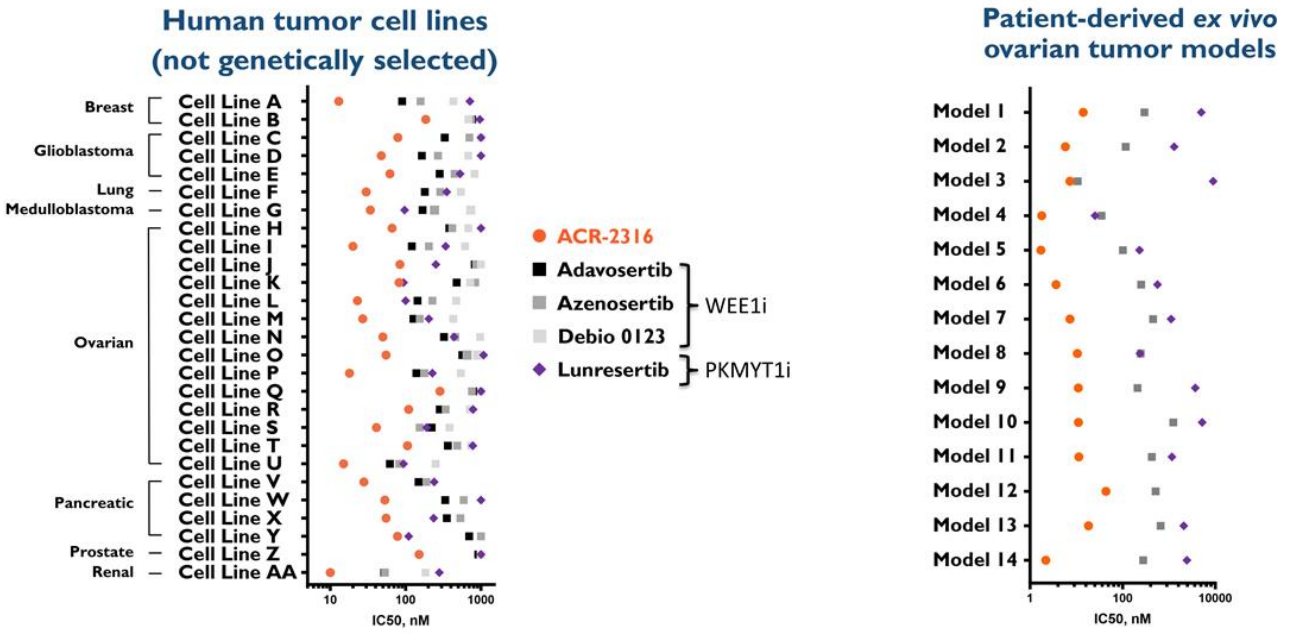


Zhu et al, J. Med. Chem. (2017)

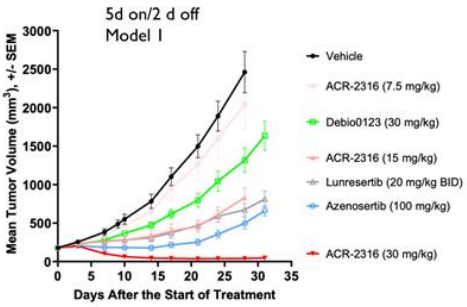
ACR-2316: Rationally designed WEE1/PKMYT1 inhibitor

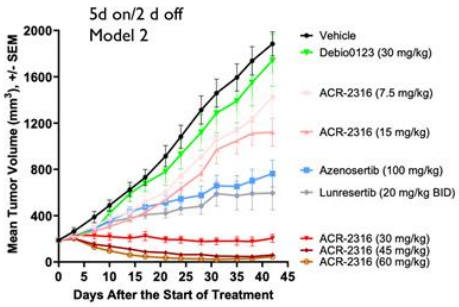
- ✓ Superior anti-tumor efficacy with complete tumor regression across models
- ✓ High selectivity ensures transient, short-lived, mild AEs
- ✓ Potent WEE1 inhibition, balanced PKMYT1 inhibition, overcomes resistance and enables robust activation of CDK1, CDK2, and PLK1 for mitotic catastrophe

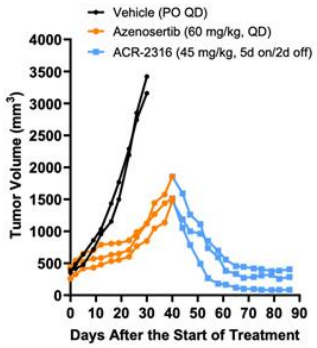
ACR-2316 IS HIGHLY POTENT ACROSS HUMAN TUMOR CELL LINES AND PATIENT-DERIVED *EX VIVO* TUMOR MODELS

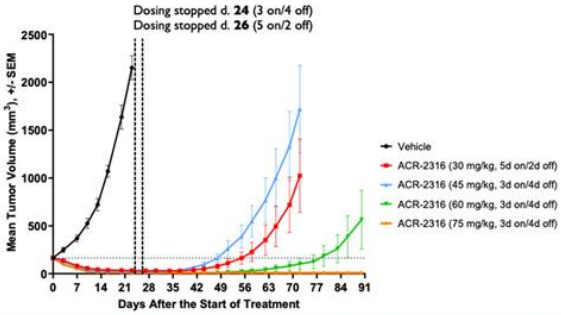


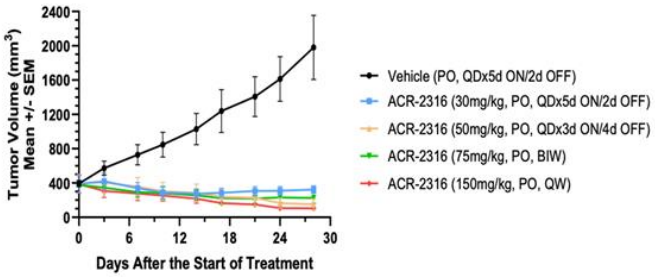
ACR-2316 INDUCES COMPLETE TUMOR REGRESSION ACROSS MODELS AND DOSING REGIMENS











ACR-2316 - FAVORABLE PRECLINICAL SAFETY PROFILE

Mice:

- ACR-2316 was well-tolerated, resulting in tumor regression in xenograft mouse models at multiple dosing regimens (qw, 2qw, 3d on/4d off, 5d on/2d off, and qd)
- Transient, reversible, mechanism-based hematological adverse events

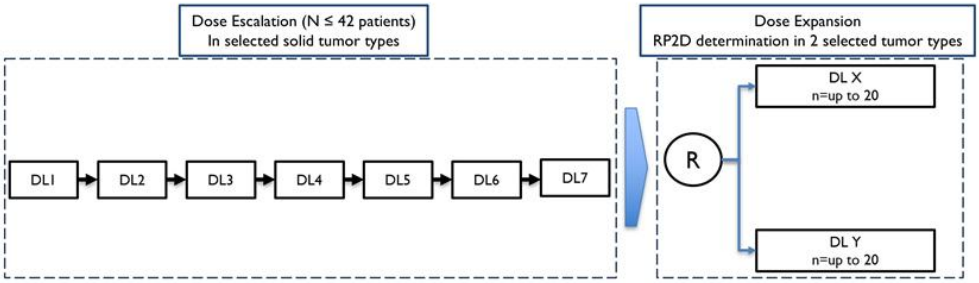
Rat and dog MTD, DRF, and GLP tox studies:

- GLP tox studies (31 days) completed in rat and dog with the planned human dosing regimen achieving exposure required for tumor regression
- Adverse events were mechanism-based, short-lived, reversible and limited to dividing myeloid progenitors and gastrointestinal tract

We believe the broad therapeutic index observed across all our preclinical studies conducted with the planned dosing regimen is consistent with the target human exposure required for anti-tumor activity and anticipated reversibility of mechanism-based AEs

ACR-2316 IND CLEARED AND INITIAL CLINICAL SITES ACTIVATED

ACR-2316-101: Phase 1 study of ACR-2316 in subjects with advanced solid tumors



Aiming for streamlined clinical development:

- Multiple sites currently activated and screening, first dosing expected shortly
- AP3-based indication finding and OncoSignature development ongoing
- Dose optimization to be guided by drug target engagement aligned with Project Optimus

ACR-2316 IS A POTENTIALLY BEST-IN-CLASS AGENT RATIONALLY DESIGNED USING ACRIVON'S AP3 PLATFORM

Program Goals		Demonstrated Preclinical Results
1 Superior single agent activity	AP3-Enabled SAR	▪ Superior* single agent anti-tumor activity through robust CDK1, CDK2, and PLK1 activation and elimination of dominant resistance mechanisms through balanced WEE1 and PKMYT1 inhibition
2 High selectivity and potency		▪ 5-20-fold more potent* in preclinical models than clinical benchmarks
3 Favorable safety profile		▪ High selectivity results in adverse events limited to transient, short-lived, mechanism-based, reversible
4 Streamlined clinical development		▪ Broad preclinical therapeutic index and anti-tumor activity across dosing regimens ▪ AP3-based identification of PD biomarkers and prioritization of promising indications

*Head-to-head preclinical studies against benchmarks with clinical data

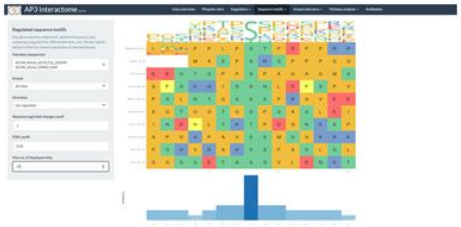
AP3 INTERACTOME V.2: PROPRIETARY INTERACTIVE DATA ANALYSIS INFRASTRUCTURE

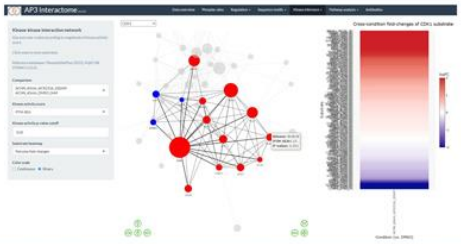
Actionable data across all AP3 experiments accessible for all Acrivon scientists
Fully scripted, algorithm-based machine learning-enabled pathway and biomarker analyses

~150,000 phosphosites

~50,000 phosphosites

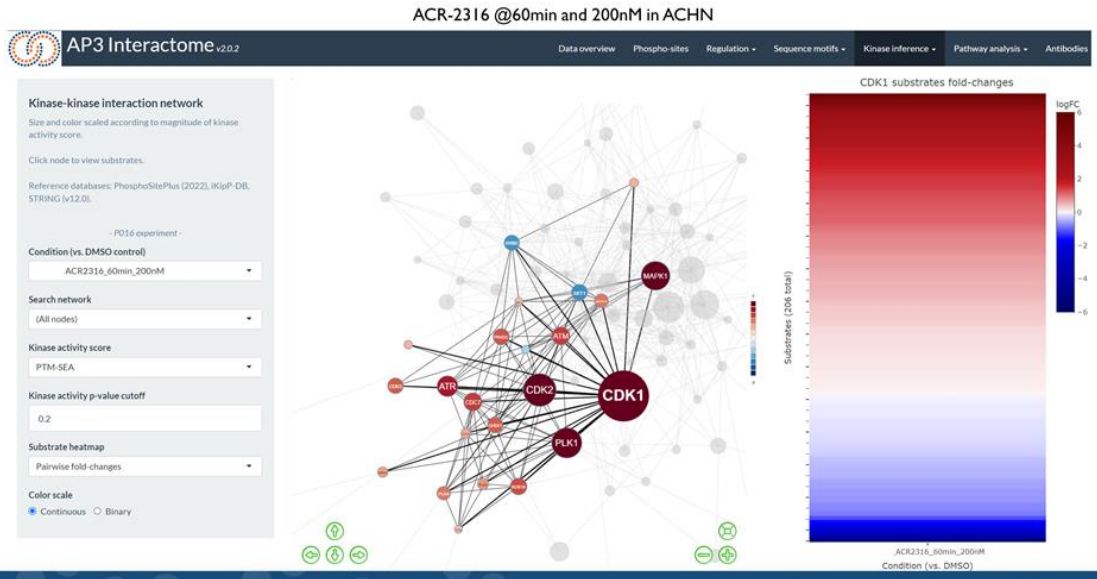
Data completeness Peptide IDs CV | Pearson Correlation | PCA Hierarchical Clustering | Filtering Batch effects Normalization Imputation | ANOVA Hierarchical clustering | DEPs Volcano Plots | Consensus Sequence Motif | Pathway Enrichment | Kinase Inference | Network Mapping | Biomarkers





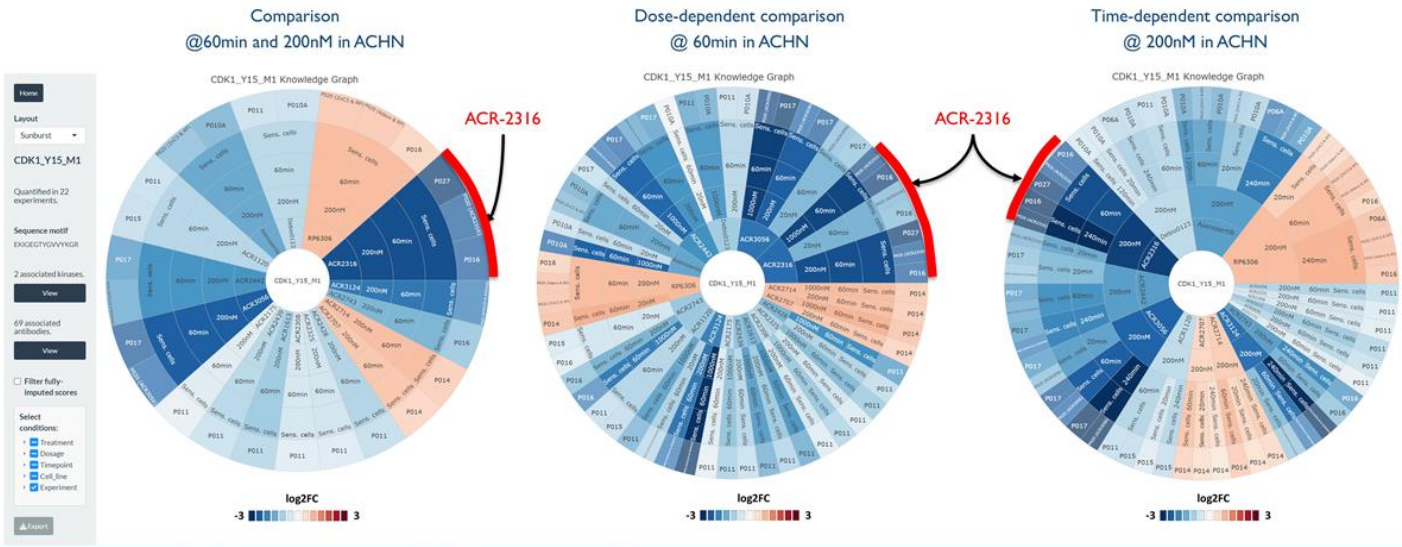
ACR-2316 INDUCES POTENT ACTIVATION OF PRO-APOPTOTIC MITOTIC KINASES IN SENSITIVE TUMOR CELLS

- Robust activation of CDK1with ACR-2316 exemplified by enrichment of 206 upregulated substrates of CDK1

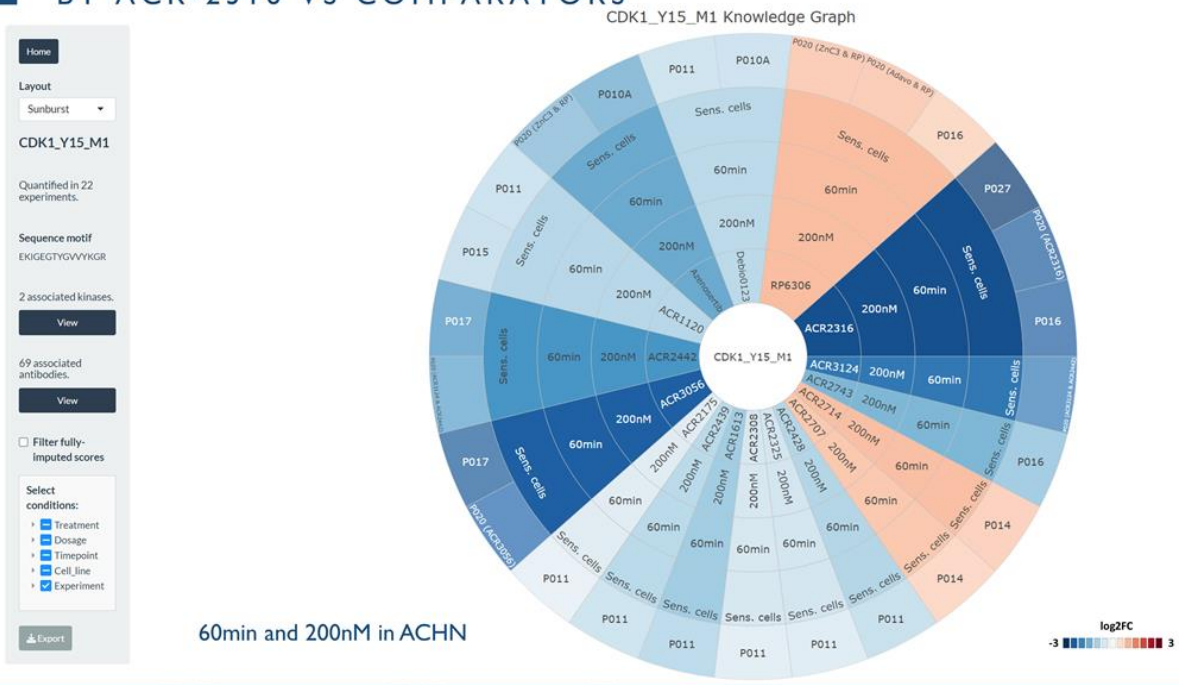


ROBUST POTENT INHIBITION OF CDK1 CONSENSUS SUBSTRATE Y15 BY ACR-2316

- AP3 interactome enables real time quantitative computational analyses of proprietary AP3 drug profiling data across different conditions and experiments

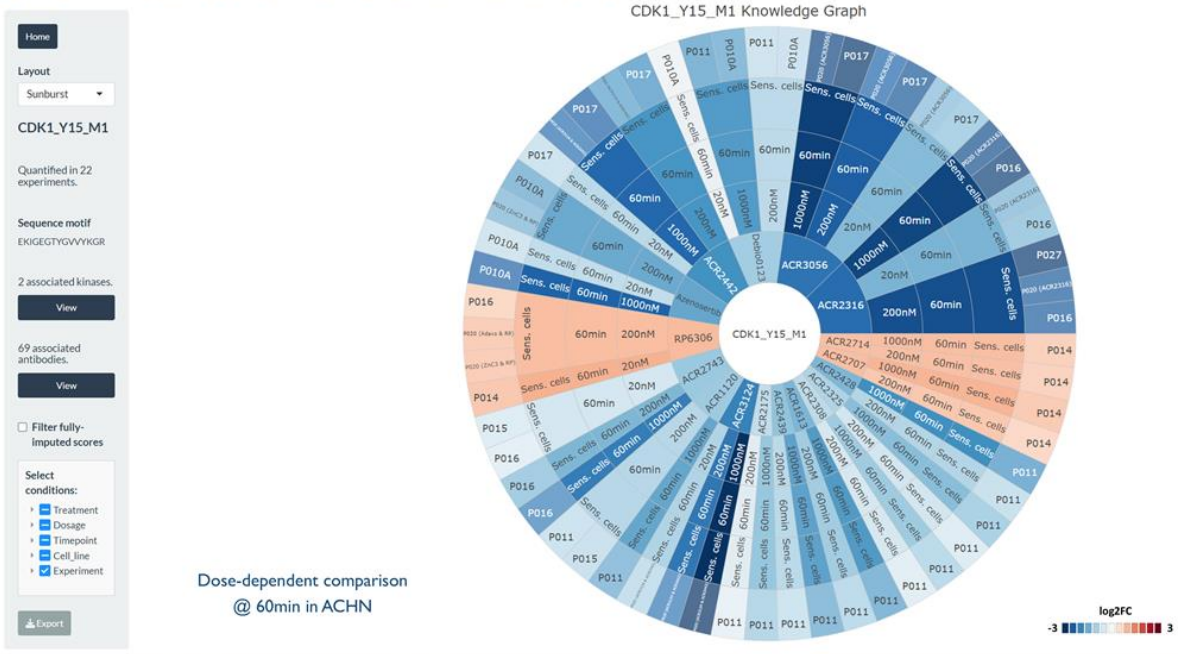


ROBUST POTENT INHIBITION OF CDK1 CONSENSUS SUBSTRATE Y15 BY ACR-2316 VS COMPARATORS



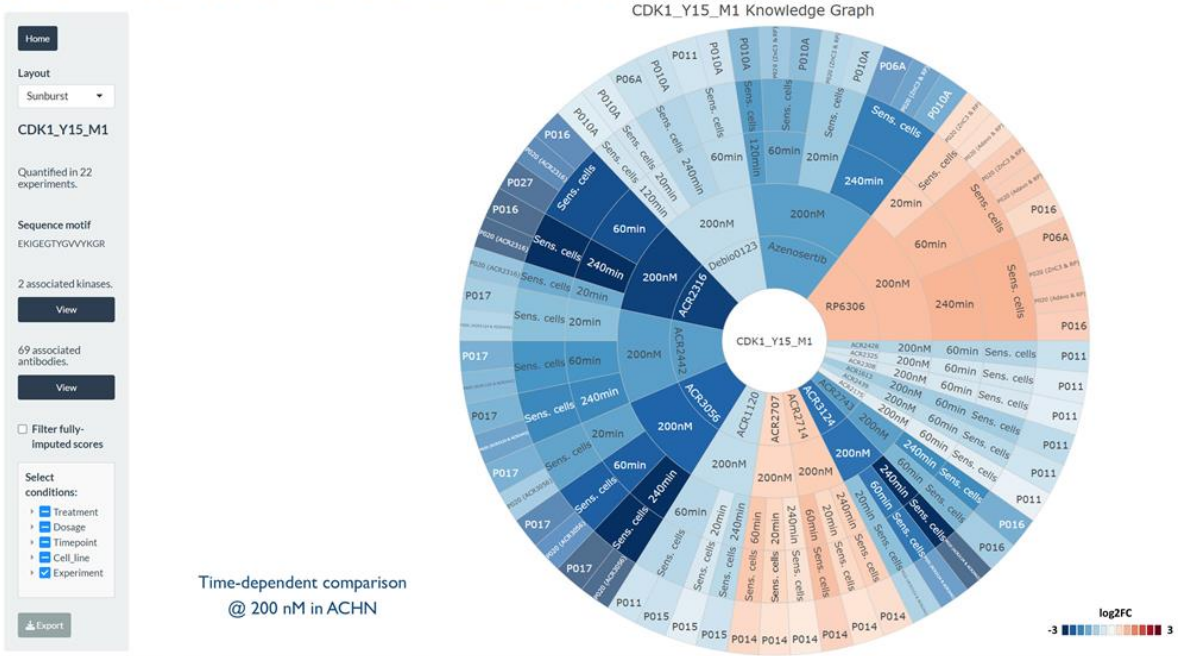
60min and 200nM in ACHN

ROBUST POTENT INHIBITION OF CDK1 CONSENSUS SUBSTRATE Y15 BY ACR-2316 VS COMPARATORS



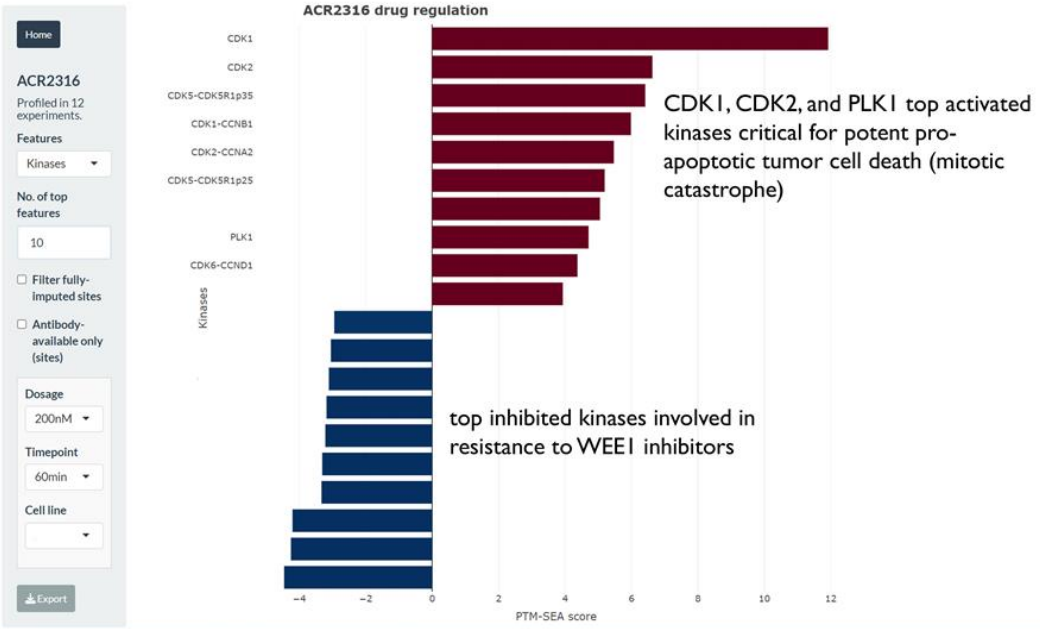
Dose-dependent comparison
@ 60min in ACHN

ROBUST POTENT INHIBITION OF CDK1 CONSENSUS SUBSTRATE Y15 BY ACR-2316 VS COMPARATORS



Time-dependent comparison
@ 200 nM in ACHN

AP3-BASED COMPOUND DESIGN IN INTACT CELLS: OPTIMAL ACTIVATION AND INHIBITION OF CRITICAL PATHWAYS



FINANCIAL HIGHLIGHTS

Cash and marketable securities

$220.4M

Balance sheet 30-June-2024

Projected runway into

H2'26

Current operating plan, assuming no additional financing

Fully Diluted Shares Outstanding

43.9M

Including shares, pre-funded warrants and equity grants outstanding 30-June-2024

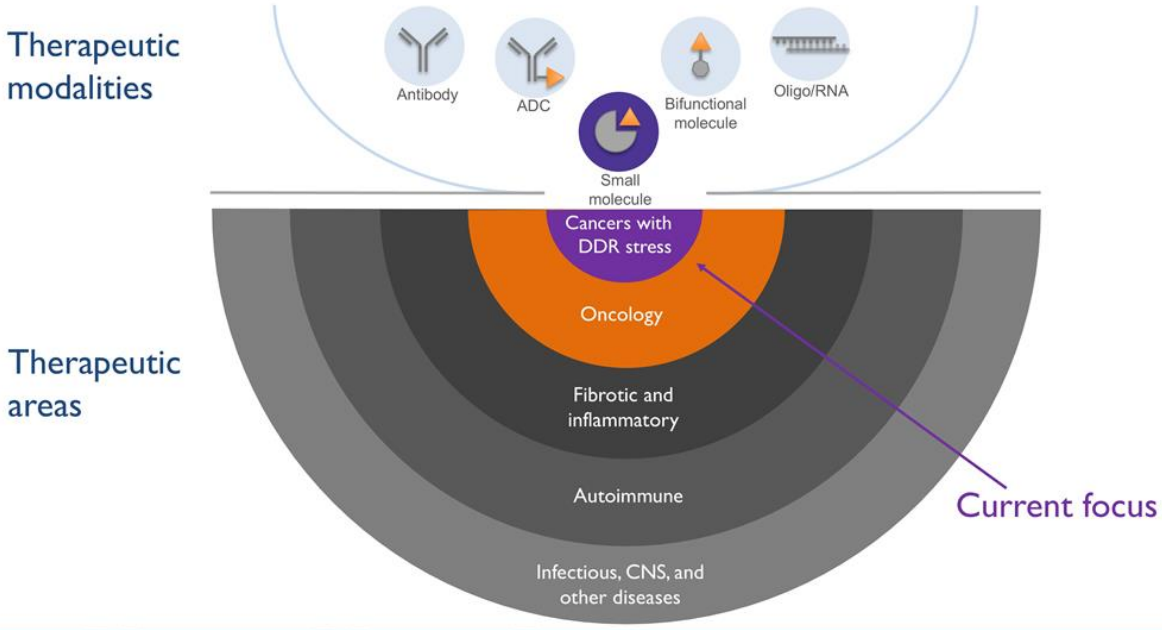
KEY TAKE AWAYS

Significant clinical advancements and continued prospective validation of our AP3 platform since last R&D update in April

1. Interim registrational intent Phase 2 clinical data for ACR-368 endometrial cancer cohort*, with confirmed ORR (63%) and lower bound of confidence interval (~30%), solidifying endometrial cancer as likely first indication for potential approval
2. Statistically significant segregation of responders in BM+ vs BM- subgroups based on prospective OncoSignature patient selection (p-value = 0.009)
3. ACR-368 endometrial cohort data maturing with all responders still on therapy; mDoR not yet reached (~6 months at time of data-cut)
4. Actively evaluating potential confirmatory trial designs for a potential future label expansion
5. IND clearance of ACR-2316, a potential best-in-class, dual WEE1/PKMYT1 inhibitor rationally designed using AP3; clinical sites activated and screening patients for enrollment in a Ph1b study
6. AP3 Interactome generating proprietary, actionable insights, leveraging in-house data and delivering fully scripted, algorithm-based machine learning-enabled pathway and biomarker analyses
7. Cash and marketable securities ~$220M with runway projected into second half of 2026

* Data cut as of July 25, 2024

THE AP3 APPROACH IS MODALITY AND DISEASE AGNOSTIC



- **Q&A session**