Acrivon Therapeutics

ACRIVON PREDICTIVE PRECISION PROTEOMICS (AP3)

NEXT GENERATION PRECISION MEDICINE

CORPORATE PRESENTATION

SEPTEMBER 2026

FORWARD-LOOKING STATEMENTS

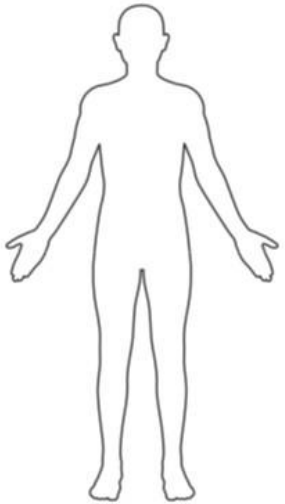
Certain information contained in this presentation includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations. 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.

Note: Acrivon intends to use its website as a means of disclosing material non-public information and for complying with its disclosure obligations under Regulation FD. For more information, please visit www.acrivon.com and follow the company on LinkedIn.

NEXT-GENERATION PRECISION MEDICINE POWERED BY AP3

Current focus oncology,
I&I next





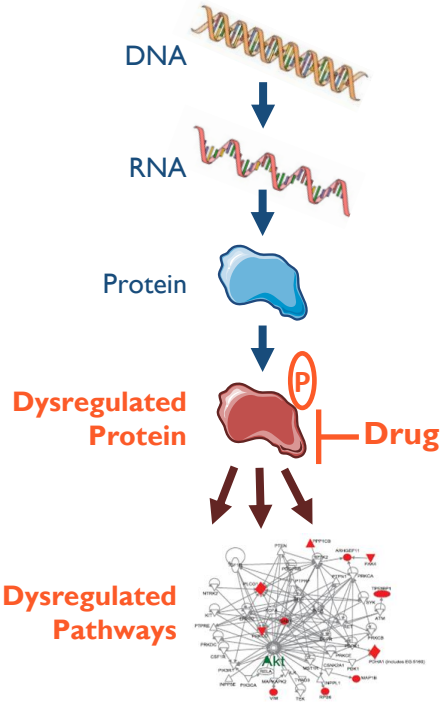
Fibrosis



Cancer

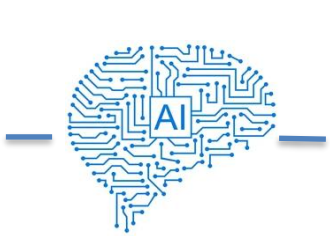


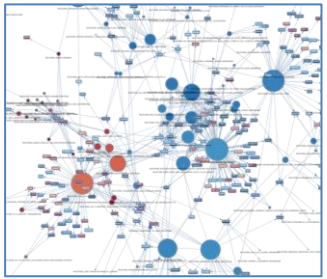
Inflammation



Acrivon Predictive Precision Proteomics (AP3)

- AI-driven, proteomics-based rational drug design and informed clinical development
- AP3 enables an exact match between the disease-driving, dysregulated pathways with drug mechanism of action (Acrivon meaning ≈ exact, accurate)





Proprietary tools

- Data portal
- Interactome
- Protein activity predictor

ACRIVON THERAPEUTICS OVERVIEW

Development Site (Boston)
- **Drug development and clinical biomarkers**
- **Clinical leadership and trial oversight**
- **ML/AI-driven AP3 analyses**

HQ LOCATED IN BOSTON - ACCESS TO LEADING DRUG DISCOVERY, BIOTECH, AND PHARMA





Precision Proteomics Site (Lund/Copenhagen)
- **Early drug discovery**
- **BM identification and drug profiling**
- **AP3 mass spectrometry**

PROTEOMIC HUB LOCATED IN MEDICON VALLEY - NORTHERN EUROPE`S LEADING LIFE SCIENCE CLUSTER





Founders



Peter Blume-Jensen, MD, PhD
CEO, President, Co-Founder
Inventor of AP3



Kristina Masson PhD, MBA
EVP, Bus Ops, Lund Site Head
Co-Founder



Jesper V. Olsen PhD
Prof., Exec. Director Novo-Nordisk Foundation Protein Center, Cph. (NNF-CPR)
Academic Co-Founder.

Founded 2018, IPO 2022 (NASDAQ:ACRV)

ACCOMPLISHED LEADERSHIP TEAM



Peter Blume-Jensen, M.D., Ph.D.
CEO, President, Co-Founder

- Executive Serono, Merck & Co., Daiichi Sankyo
- CSO Metamark - Marketed prostate proteomic test ProMark®
- Inventor Acrivon Predictive Precision Proteomics (AP3)



Mansoor Raza Mirza, M.D.
Chief Medical Officer

- World-renowned oncology KOL
- Lead investigator for multiple guideline-changing regulatory approvals, including PARP inhibitors for ovarian cancer and new frontline therapy for endometrial cancer



Kristina Masson, Ph.D., M.B.A
Site Head Acrivon AB, Co-Founder
EVP Business Operations

- Cross-functional Leadership Merrimack Pharmaceuticals, MIT/BROAD
- Founder and CEO, OncoSignature AB (acquired by Acrivon Therapeutics)



Adam Levy, Ph.D., M.B.A.
Chief Financial Officer

- Zentalis Pharmaceuticals, Turning Point Therapeutics, Novartis
- Head of Corporate Strategy Gilead Sciences
- Engagement manager in pharma practice at McKinsey & Company



Eric Devroe, Ph.D.
Chief Operating Officer

- Founder and CEO, Opsonix
- Business executive MD Anderson Cancer Center and Metamark
- EIR Wyss Institute, Harvard
- Associate, Flagship Pioneering



Michaela Levin, Ph.D.
Chief Business Officer

- VP, BD at Recursion
- Senior BD roles at Editas, Ovid, and Constellation
- BD/Licensing tech transfer roles at Mass General Brigham and Harvard



Erick Gamelin, M.D., Ph.D.
Chief Development Officer

- Professor, CEO, national cancer center, appointed by French Minister of Health
- Executive Amgen, Pfizer, Dynavax, MacroGenics; CMO STEP Pharma
- >100 ph 1-3 oncology trials

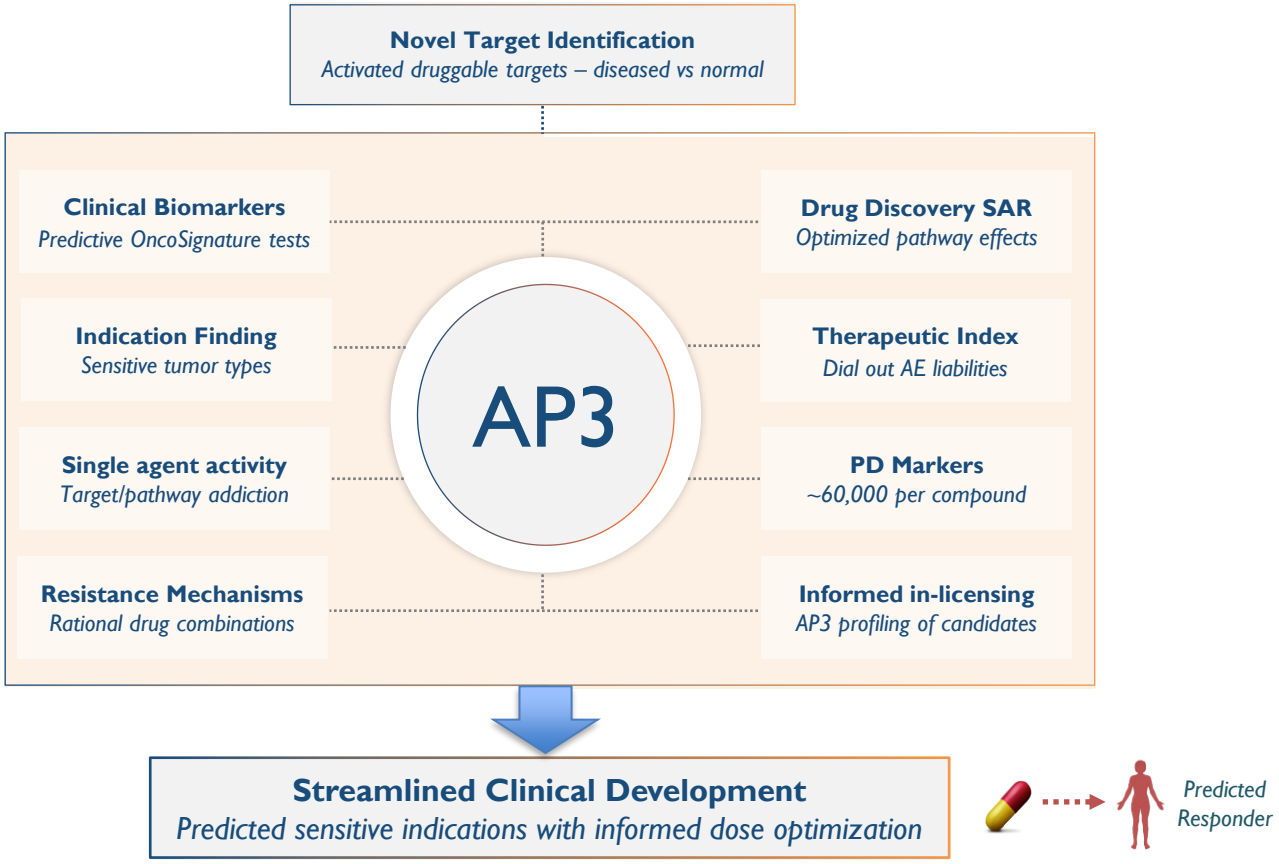


Mary-Alice Miller, J.D.
Chief Legal Officer

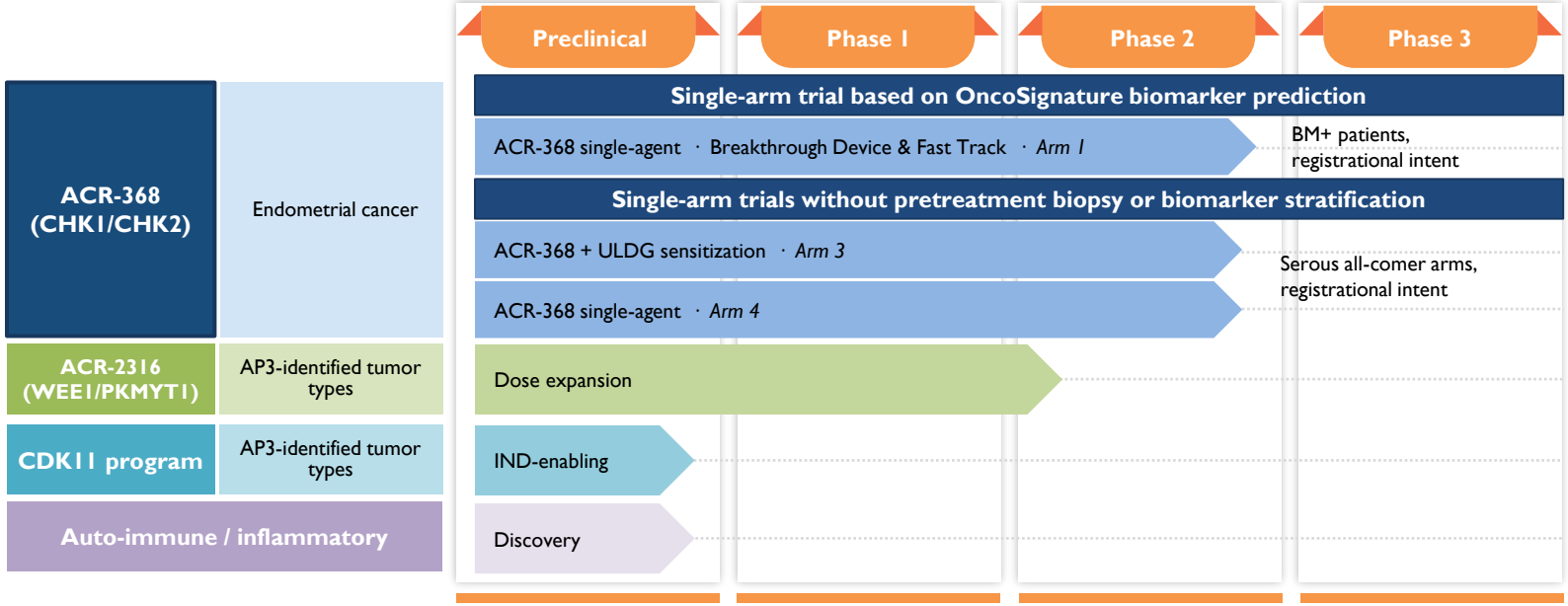
- Over 20 years corporate legal experience
- Served as general counsel of 2 companies taken public
- Boston Business Journal “40 Under 40”

ACRIVON AP3-BASED PRECISION MEDICINE

A REITERATIVE ENGINE DEVELOPED FOR RAPID CLINICAL POC



OUR PIPELINE



UPCOMING MILESTONES

ACR-368 (Phase 2b)

- Prespecified simultaneous interim analysis and data update from both all-comer (biopsy-independent) serous EC arms of the ACR-368 Phase 2b study in second half of 2026
- Initiate Phase 3 confirmatory trial for ACR-368 in first half of 2027
- Based on interim data read-out, complete enrollment of the registrational intent all-comer (biopsy-independent) serous EC Arm 3 or Arm 4 by fourth quarter of 2026

ACR-2316 (Phase 1/2)

✓ Additional ACR-2316 Phase 1/2 clinical data for weekly and bi-weekly dosing regimens and transition into dose expansion in AP3-identified tumor types in 2026

Earlier Pipeline

- Submit IND filing to the FDA for CDK11 inhibitor development candidate in first half of 2027
- Initiate additional internal programs utilizing the AP3 platform in 2026

ACRIVON CLIA LABORATORY

STRENGTHENING ACRIVON PRECISION MEDICINE CAPABILITIES

- Newly licensed CLIA laboratory
- Translates AP3-driven biomarker discoveries into actionable and proprietary CDx for our therapeutics
- Initially focused on ACR-368 OncoSignature testing
- Unique capabilities to support internal pipeline and strategic BD/partnerships





CENTERS FOR MEDICARE & MEDICAID SERVICES
CLINICAL LABORATORY IMPROVEMENT AMENDMENTS

CERTIFICATE OF REGISTRATION

LABORATORY NAME AND ADDRESS
ACRIVON THERAPEUTICS, INC
480 ARSENAL WAY, SUITE 100
WATERTOWN, MA 02472

CLIA ID NUMBER
22D2334886

EFFECTIVE DATE
12/03/2025

LABORATORY DIRECTOR
THOMAS P. NIFONG

EXPIRATION DATE
12/02/2027

Pursuant to Section 353 of the Public Health Services Act (42 U.S.C. 263a) as revised by the Clinical Laboratory Improvement Amendments (CLIA), the above named laboratory located at the address shown herein (and other approved locations) may accept human specimens for the purposes of performing laboratory examinations or procedures.
This certificate shall be valid until the expiration date above, but is subject to revocation, suspension, limitation, or other sanctions for violation of the Act or the regulations promulgated thereunder.

CMS

Gregg Brandish, Director
Division of Clinical Laboratory Improvement & Quality
Quality & Safety Oversight Group
Center for Clinical Standards and Quality



The Commonwealth of Massachusetts

DEPARTMENT OF PUBLIC HEALTH

DIVISION OF HEALTH CARE FACILITY LICENSURE AND CERTIFICATION

CLINICAL LABORATORY LICENSE

In accordance with the provisions of the General Laws, Chapter 111D and regulations established thereunder, a license is hereby granted to

ACRIVON THERAPEUTICS, INC.
480 ARSENAL WAY, SUITE 100, WATERTOWN MA 02472

for the maintenance of

ACRIVON THERAPEUTICS, INC
480 ARSENAL WAY, SUITE 100, WATERTOWN MA 02472

5822

Classification: FULL

Pathology

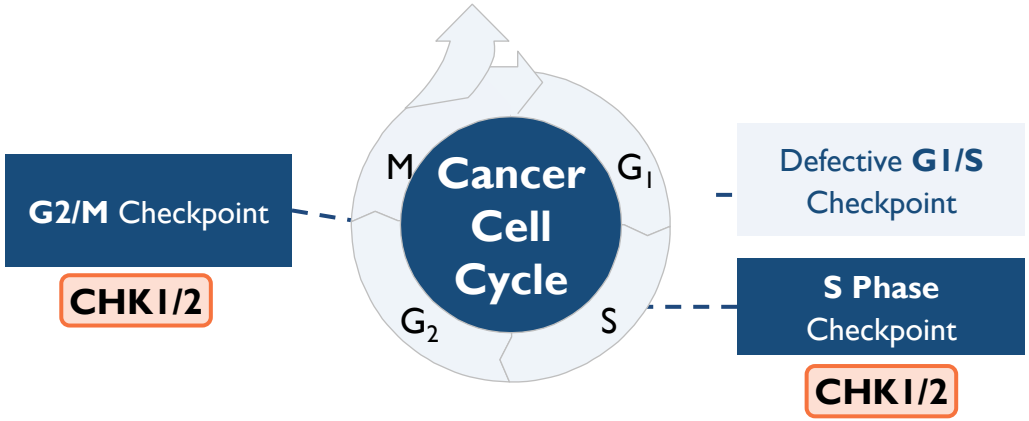
LICENSE № 5822 is valid from December 30, 2025 to December 29, 2027 subject to revocation for cause.

December 30, 2025

POST CONSPICUOUSLY

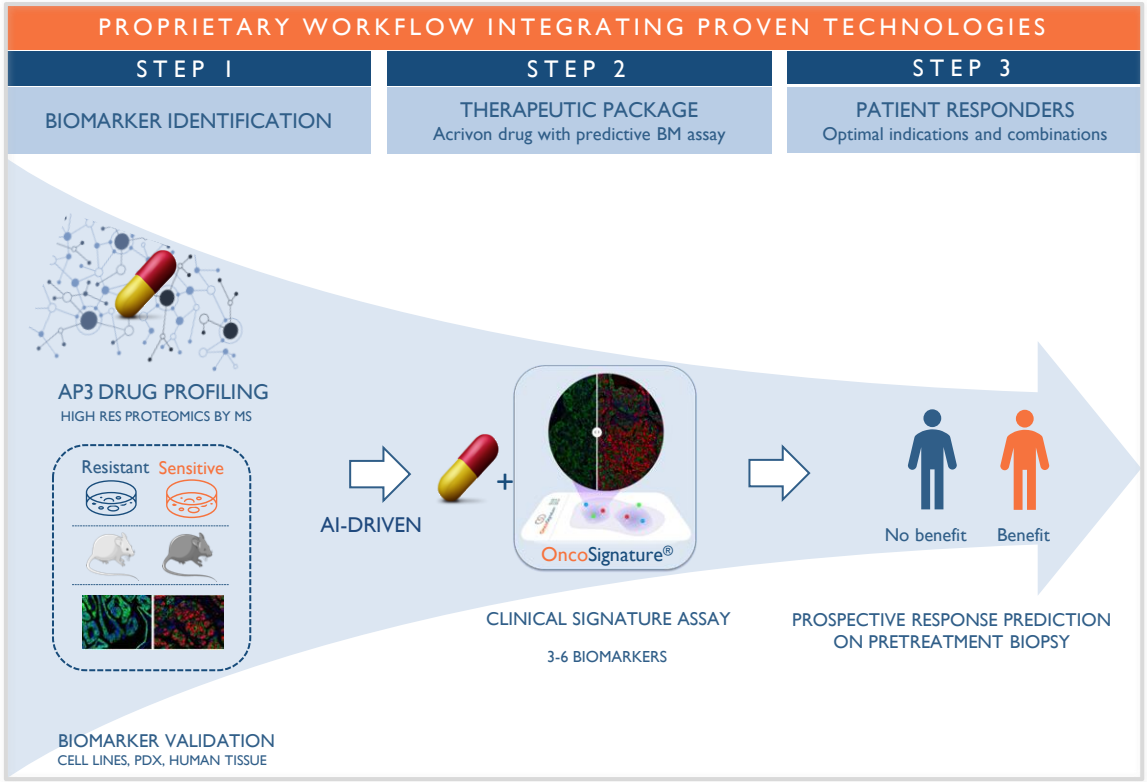
ACR-368: A POTENT SELECTIVE CHK1/2 INHIBITOR

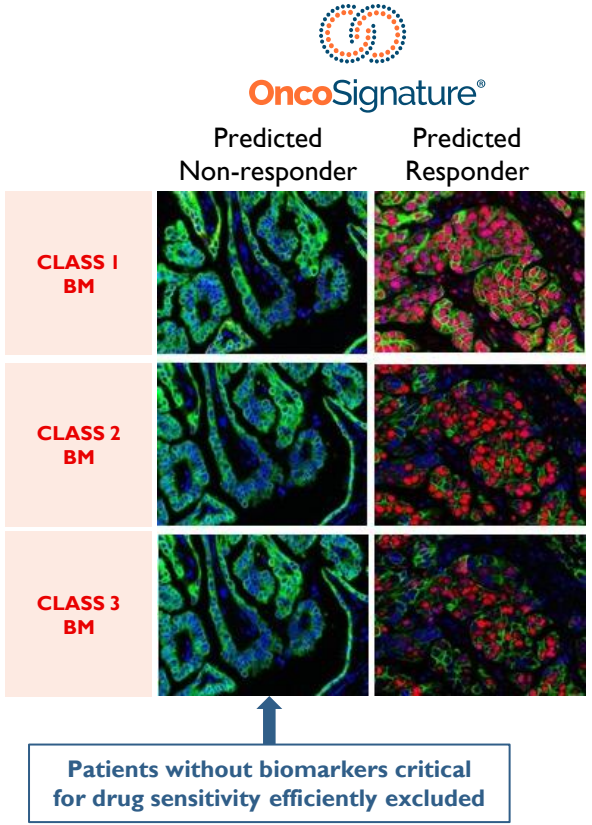
- **Clinical efficacy and safety:** Durable monotherapy activity across multiple cancers with favorable tolerability and absence of non-hematological, severe toxicities
- **AP3 Indication Finding:** Endometrial cancer was identified as a tumor type predicted to be sensitive to ACR-368
- **Synergy with both immune checkpoint inhibitors and TOPO1 inhibitors:** Strong preclinical data and rationale support potential for confirmatory Phase 3 combination studies



- **Potent inhibition:** Balanced potent (nM) inhibition of CHK1 and CHK2 enabling monotherapy activity
- **IP:** Protected by composition-of-matter and lactate form patents through 2030 and 2037, ensuring exclusivity

ONCOSIGNATURE: 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*

AP3 INDICATION FINDING IDENTIFIES ENDOMETRIAL CANCER AS A NEW TUMOR TYPE SENSITIVE TO ACR-368

ACR-368 OncoSignature-based indication finding prior to trial entry

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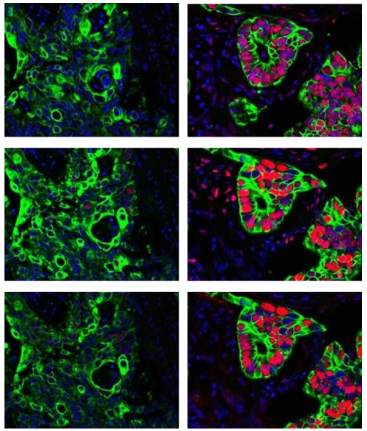
Functional validation in preclinical models

→

Clinical validation in ongoing Phase 2b study

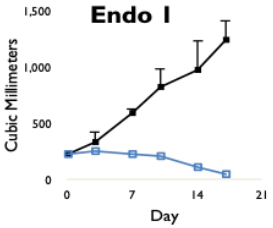


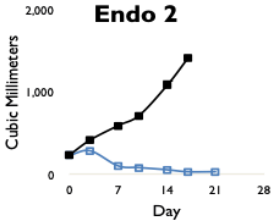
Endometrial patient tumor samples

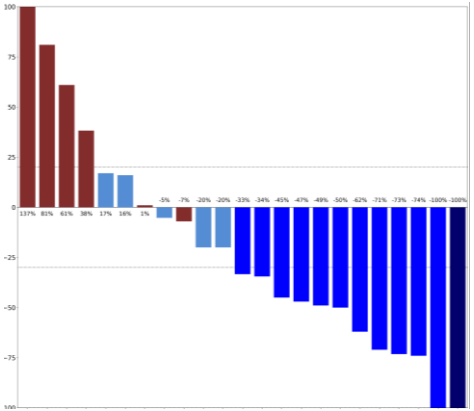


Predicted Non-Responder

Predicted Responder

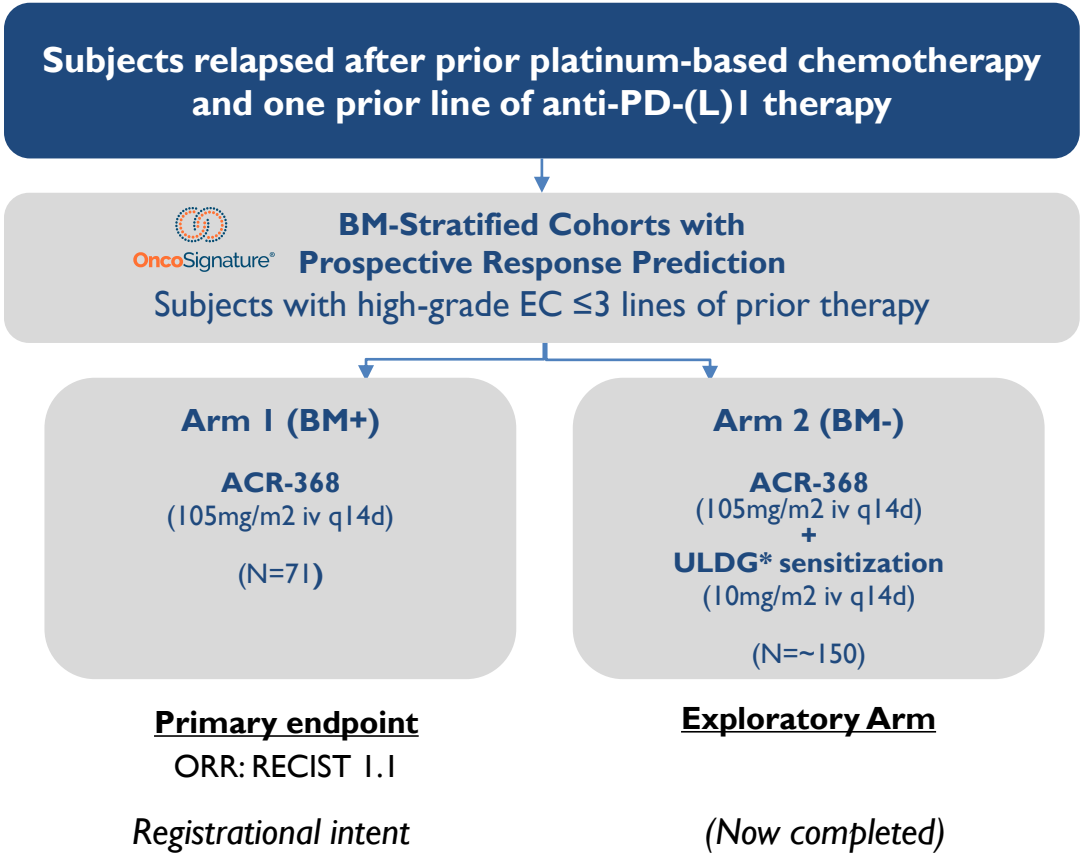






INITIAL TRIAL DESIGN

- The ACR-368 OncoSignature is a tumor agnostic Biomarker (BM) test designed to prospectively predict benefit from ACR-368 (prexasertib), a potent, selective CHK1/2 inhibitor.
- It measures the tumor's addiction to CHK1/2-mediated DNA repair independent of genetic alterations.
- Screening with Acrivon's OncoSignature BM test across routine-processed (FFPE) human tumor types, predicted endometrial cancer (EC) to be particularly sensitive to ACR-368.



*ULDG = ultra low dose gemcitabine

FAVORABLE SAFETY PROFILE

- Limited, transient, mechanism-based hematological AEs
- **Notable Absence of**
  - GI toxicities, ILDs, stomatitis, ocular toxicity, peripheral neuropathy, etc.

Treatment-Related Adverse Events ***N = number of subjects (%)***	**Arm 1** (ACR-368) **N=40** **Grades 3/4**	**Arm 2** (ACR-368 + ULDG) **N=48** **Grades 3/4**
Thrombocytopenia	9 (22)	17 (34)
Anemia	11 (27)	22 (46)
Leukopenia	6 (15)	11 (23)
Neutropenia	10 (25)	16 (33)
Febrile neutropenia	2 (5)	4 (8)
Acute kidney injury	2 (5)	0

TRAEs with Grades 3/4 percentages ≥5% for either group are included in this table. No fatal TRAE in either group.
G-CSF is encouraged for ACR-368 monotherapy and mandated for ACR-368 + ULDG

Data-cut of 01/13/2026

ENDOMETRIAL PATIENT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Subject Demographics	BM+ N = 40	BM- N = 48
Median Age (range)	66.0 (40, 77)	66.0 (49, 80)
Race, n (%)		
White	29 (72.5)	29 (60.4)
Black/African American	6 (15)	10 (20.8)
Asian	1 (2.5)	4 (8.3)
American Indian or Alaska Native	0	0
Native Hawaiian or other pacific islander	1 (2.5)	0
Other/Unknown	3 (7.5)	5 (10.4)
Stage, n (%)		
III	10 (25)	18 (37.5)
IV	30 (75)	29 (60.4)
Unknown	0	1 (2.1)
Histology, n (%)		
Serous	**20 (50)**	**16 (33.3)**
Clear-cell carcinoma	2 (5)	4 (8.3)
Carcinosarcoma	6 (15)	10 (20.8)
Endometrioid, G3	9 (22.5)	15 (31.3)
Other	3 (7.5)	3 (6.3)
ECOG Status at Baseline, n (%)		
0	20 (50)	25 (52)
1	20 (50)	23 (48)

Subject Demographics	BM+ N = 40	BM- N = 48
Prior Lines of Therapy, Median (Mean)	2 (2)	2 (2)
Best Overall Response to Last Prior Line		
Refractory	9 (22.5)	15 (31.3)
Relapsed disease	31 (77.5)	33 (68.7)
Unknown	0 (0)	0 (0)
MMR Status, n (%)		
pMMR	28 (70)	29 (60.4)
dMMR	1 (2.5)	6 (12.5)
Unknown	11 (27.5)	13 (27.1)
TP53 Status, n (%)		
Mutant	24 (60)	15 (31.3)
Wildtype	6 (15)	11 (22.9)
Unknown	10 (25)	22 (45.8)
Prior exposure to PD-1/PD-L1, n (%)		
Yes	39 (97.5)	46 (95.8)
No	1 (2.5)	2 (4.2)
Prior exposure to Pembro/Len, n (%)		
Yes	19 (47.5)	20 (41.7)
No	21 (52.5)	28 (58.3)

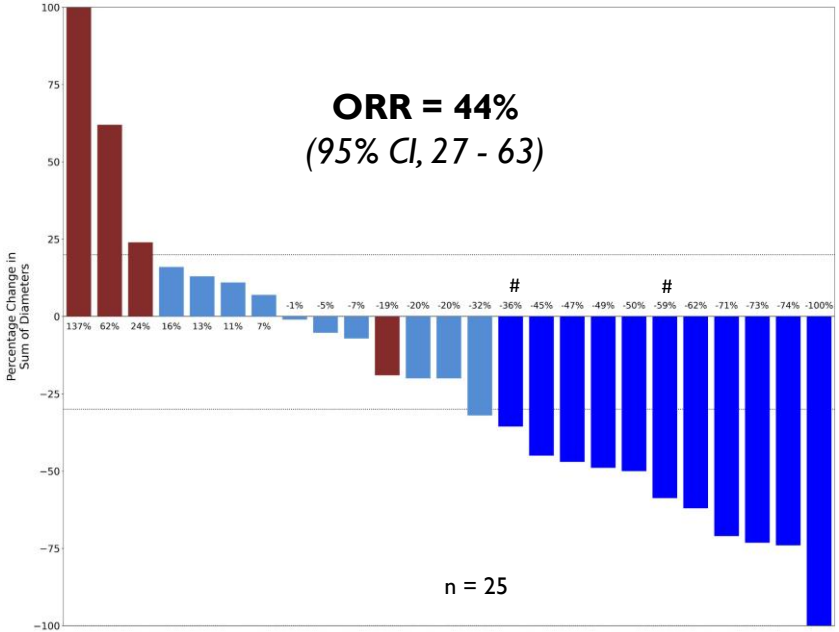
Non QC'ed data based on EDC data extract as of 01/13/2026

BETTER ORR OBSERVED IN SUBJECTS WITH ≤2 PRIOR LINES OF THERAPY

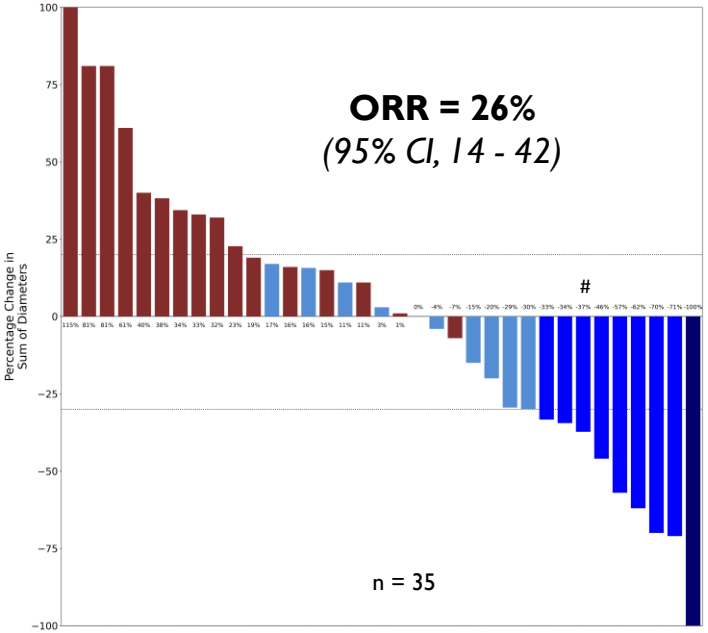
BOR by RECIST 1.1 on study treatment*

CR
PR
SD
PD

Arm 1 (BM+)
ACR-368



ARM 2 (BM-)
ACR-368 + ULDG

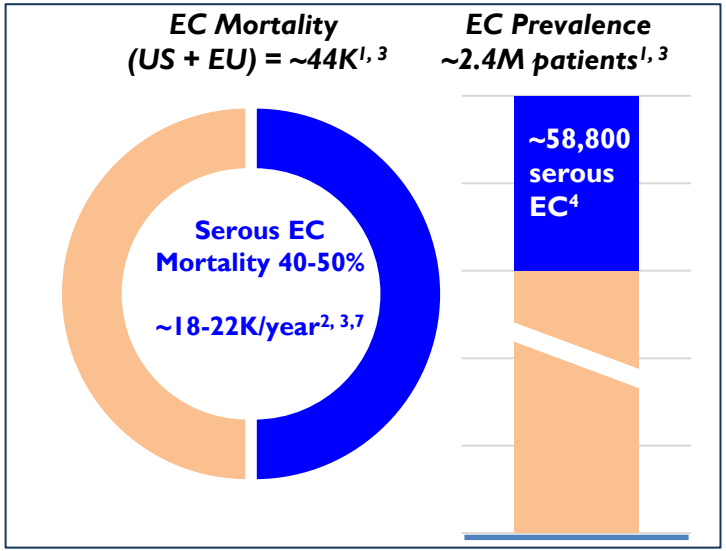


OncoSignature BM levels and the BM+ fraction were noted to be significantly higher in serous

* Best of BICR and/or PI
\# Unconfirmed PR

Non QC'ed data based on EDC data extract as of 12/04/2025

SEROUS ENDOMETRIAL CANCER - A SIGNIFICANT UNMET NEED



Disproportionate Mortality

- *Accounts for ~40-50% of all endometrial cancer deaths.[5, 8]*

Limited Effective Treatment Options

- *After frontline IO + chemotherapy, pem + len no longer viable option in ≥2L[6]*
- *Chemotherapy responses short-lived. Rapid resistance, early recurrence.*
- *HER2-targeting benefits smaller proportion, no TP53-directed therapies*

Almost all serous patients progress to ≥2L of therapy

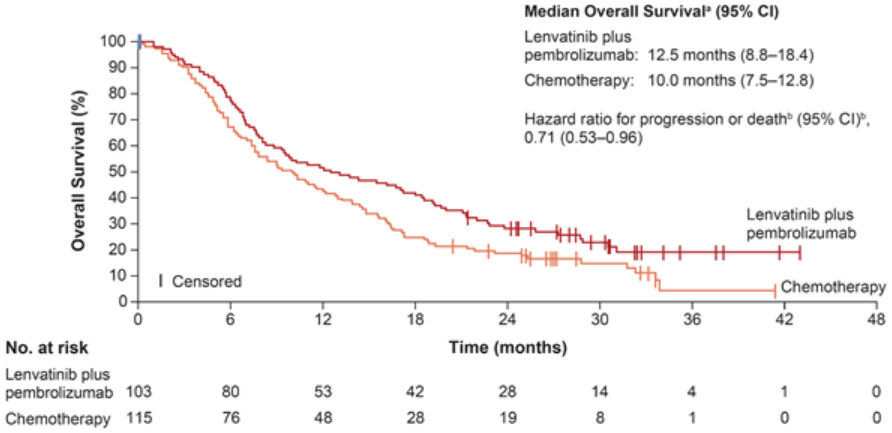
SOC in ≥2L post-IO/platinum ~13% ORR and ~3.6 months PFS and 10 months OS (single agent chemotherapy)[5, 7, 9]

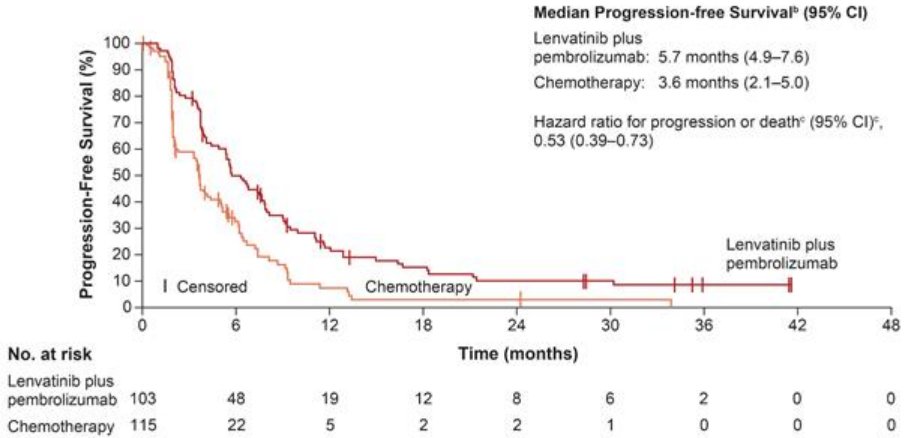
Large addressable total annual market (TAM) opportunity (US + EU)

- *Serous patients: ~(20,000 per year x >6 months mDoT)*
- *Existing high unmet need prevalence pool: additional ~60,000 patients*

[1]SEER database
[2]https://pmc.ncbi.nlm.nih.gov/articles/PMC9445918
[3]Concin, C. et al, ESGO–ESTRO–ESP 2025 Guidelines; Lian Y., Luo P. Annals of Global Health (2025).
[4]Based on internal estimates of approximately 2.4% serous in the prevalence pool given survival approximations
[5]Bogani et al, Gynecol Oncol. 2021 July ; 162(1): 226–234. doi:10.1016/j.ygyno.2021.04.029.
[6]Live KOL event during ESGO (See https://ir.acrivon.com/events/event-details/endometrial-cancer-kol-panel-discussing-acrivons-phase-2b-acr-368-study)
[7]Makker et al, NEJM; 2022; 386:437-48
[8]KOL estimates
[9]Sub-group analysis of KEYNOTE 775 data: Lorusso, Makker, et al data from ESGO 2022

SEROUS EC ALL-COMER POPULATION (KEYNOTE-775) SHOWS 3.6 MONTHS PFS AND 10 MONTHS OS IN 2ND LINE





Control arm from KEYNOTE-775 study (N = 115)

Lorusso et al, 2022

[a]From product-limit (Kaplan-Meier) method for censored data; [b]based on Cox regression model with Efron's method of tie handling with treatment as a covariate. Analyses were conducted using an unstratified Cox model.

SEROUS EC ALL-COMER POPULATION (KEYNOTE-775 CONTROL ARM) SHOWS 13% ORR

	Low-grade endometrioid		Endometrioid not further defined/not defined as low grade		Serous		Clear cell	
Parameter[a]	**LEN + pembro** (n = 59)	**Chemotherapy** (n = 54)	**LEN + pembro** (n = 185)	**Chemotherapy** (n = 200)	**LEN + pembro** (n = 103)	**Chemotherapy** (n = 115)	**LEN + pembro** (n = 30)	**Chemotherapy** (n = 17)
ORR, % (95% CI[b])	42.4 (29.6–55.9)	11.1 (4.2–22.6)	32.4 (25.7–39.7)	18.5 (13.4–24.6)	36.9 (27.6–47.0)	13.0 (7.5–20.6)	26.7 (12.3–45.9)	0 (0–19.5)
CR, %	13.6	3.7	5.9	2.5	8.7	3.5	3.3	0
PR, %	28.8	7.4	26.5	16.0	28.2	9.6	23.3	0
mDOR, mo range	20.0 (1.6–35.5+)	4.3 (3.7–31.3+)	12.7 (2.6–32.7+)	5.8 (0.0+ –37.1+)	9.0 (2.4–39.5+)	5.6 (3.2–30.2)	8.4 (4.2–28.3+)	---
DCR[c], % (95% CI[b])	81.4 (69.1–90.3)	44.4 (30.9–58.6)	72.4 (65.4–78.7)	54.0 (46.8–61.1)	73.8 (64.2–82.0)	35.7 (26.9–45.1)	56.7 (37.4–74.5)	35.3 (14.2–61.7)

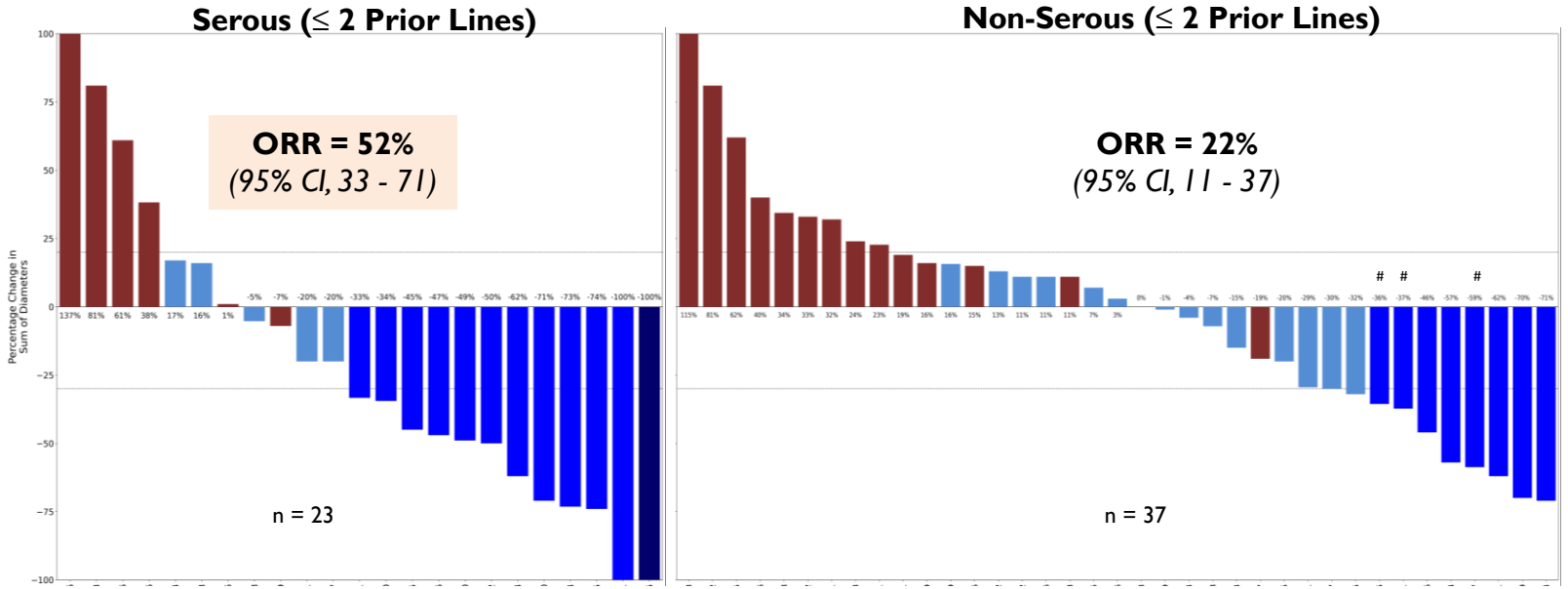
Lorusso et al, 2022

[a]By BICR per RECIST v1.1; [b]based on binomial exact confidence interval method; [c]CR + PR + SD ≥ 7 weeks.

SIGNIFICANT ORR IN SEROUS ALL-COMER POPULATION WITH ≤ 2 PRIOR LINES OF THERAPY

BOR by RECIST 1.1 on study treatment*

CR
PR
SD
PD



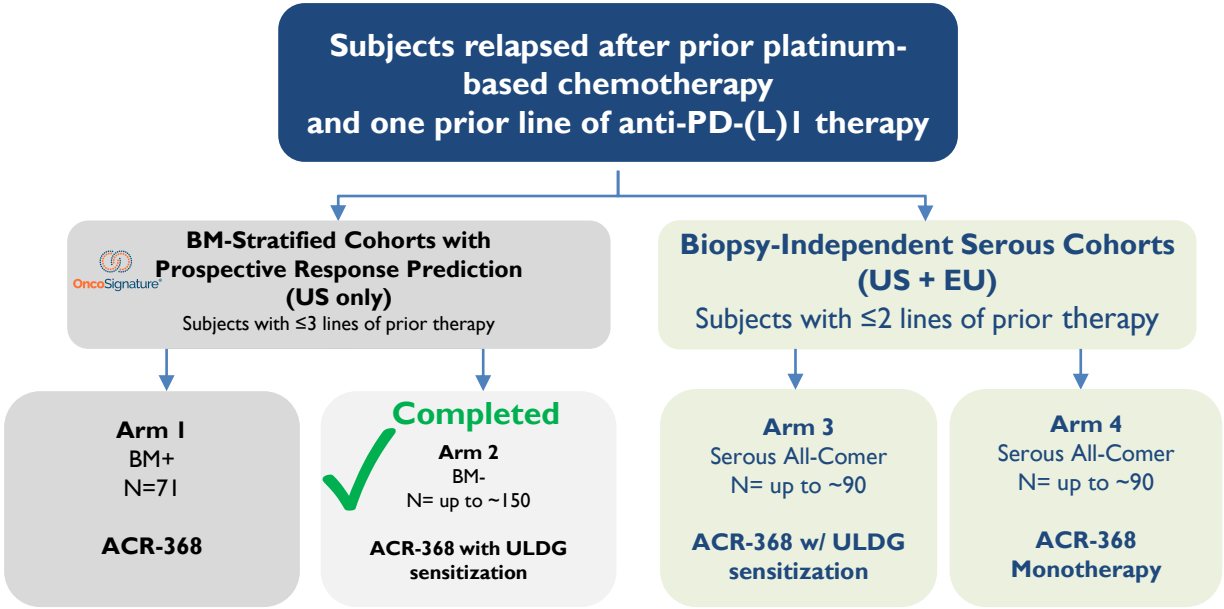
DCR: 74%, CBR (16 weeks): 65%

* Best of BICR and/or PI
\# Unconfirmed PR

Non QC'ed data based on EDC data extract as of 12/04/2025

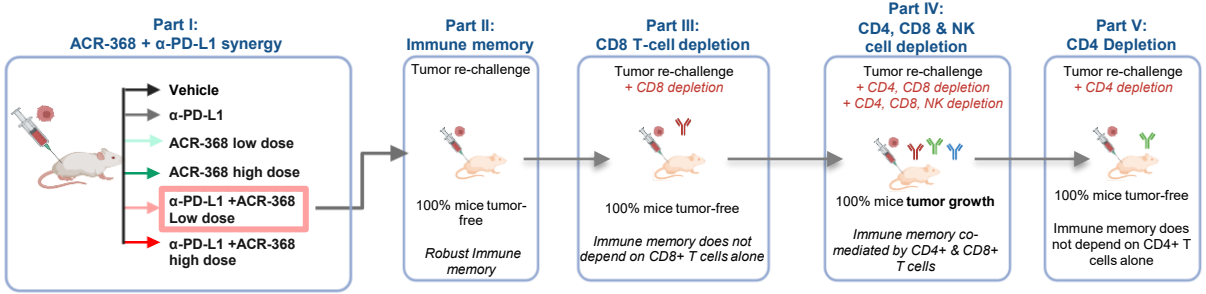
ACR-368 PROGRAM INCREASINGLY FOCUSED ON SEROUS ENDOMETRIAL CANCER

- Serous EC shows particularly high ORR in both BM+ and BM- tumors
- ACR-368 has a favorable safety profile
- Arm 3 and Arm 4 are evaluating ACR-368 + ULDG and ACR-368, respectively, in serous EC all-comer (biopsy-independent) subjects
- The study is being expanded to >20 EU sites

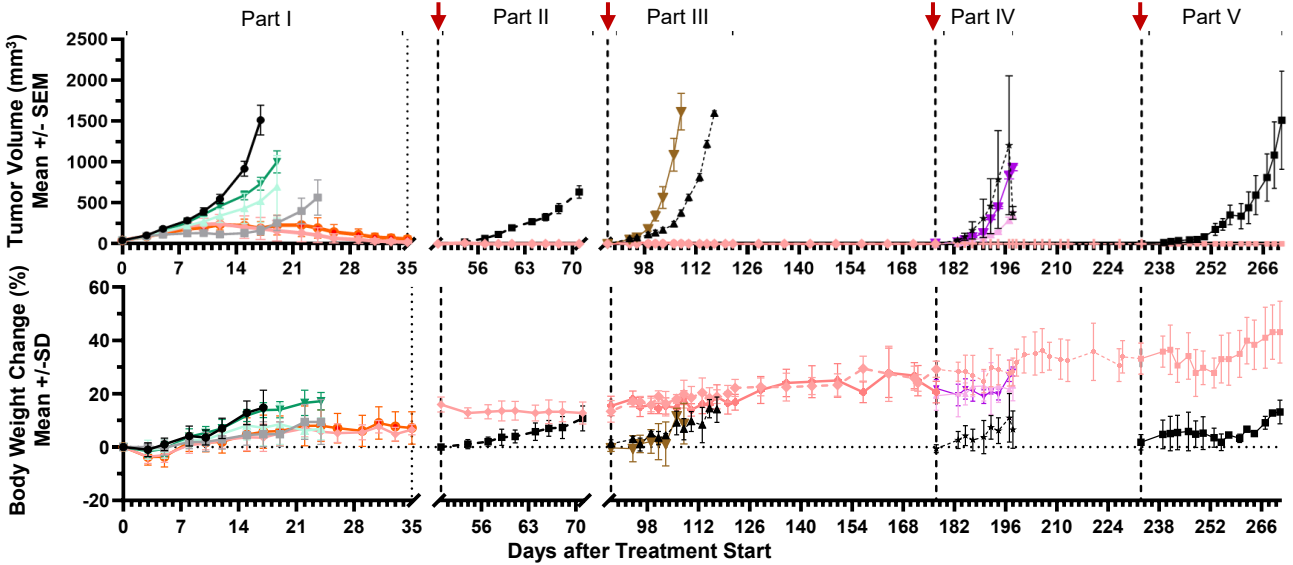


Prespecified interim analysis 2H 2026

POTENT ACR-368 + ANTI-PD-L1 SYNERGY WITH COMPLETE TUMOR REGRESSION AND IMMUNE MEMORY MEDIATED BY CD4+ AND CD8+ CELLS



Tumor cell re-challenge



AACR 2026: ACR-368 SYNERGY WITH CHECKPOINT INHIBITION

Poster # LB152

ACR-368 synergizes with PD-L1 blockade by coordinated activation of adaptive and innate immunity pathways to achieve robust anti-tumor efficacy

Amira Elbakry[1], Taronish Dubash[1], Joelle Baddour-Sousounis[1], Jessica Hopkins[1], Subodh Kumar[1], Ahmed Youssef[1], Yinghun Spring Liu[1], Kate Rappard[1], Calvin Yang[1], Ignacio Arribas Diez[2], Marc Isaksson[2], Luka Romero[1], Zachary Best[1], Nina Lipjankic[2], Sofija Skoric[2], Courtney Cooper[1], Emma Ahrman[2], Valentina Siino[2], Portia Lombardo[1], Corey Xu[1], Magnus E. Jakobsson[2], Helen Nilsson[2], Lei Shi[1], Ayesha Murshid[1], Michail Shipitsin[1], Joon Jung[1], David Proia[1], Erick Gamelin[1], Kristina Masson[1], Peter Blume-Jensen[1]

[1]Acrivon Therapeutics Inc., Watertown MA, USA; [2]Acrivon AB, Medicon Village, Lund, Sweden

Introduction

- ACR-368 is a potent and selective CHK1/2 inhibitor with demonstrated durable clinical activity which is currently being evaluated as monotherapy and in combination regimens in Acrivon Therapeutics' ongoing registrational-intent Phase 2 endometrial cancer clinical trial.
- Preclinical studies indicate that ACR-368 activates multiple anti-tumor immune responses, supporting its combination with immune checkpoint inhibitors (ICIs).
- ACR-368 in combination with anti-PD-L1 led to complete tumor regression in a syngeneic colorectal cancer mouse model and long-lasting immune memory driven by anti-tumor innate and adaptive immune responses.

Potent synergy of ACR-368 with anti-PD-L1 and induction of durable immune memory mediated by CD4+ and CD8+ cells

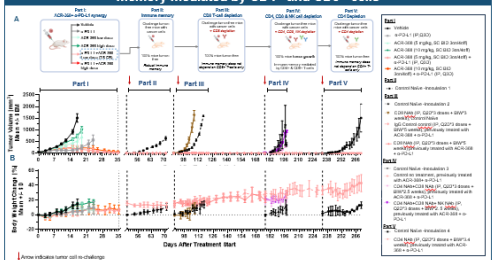


Figure 1: Complete tumor regression and durable immune memory mediated by adaptive immunity. (A) In a syngeneic colorectal cancer mouse model, ACR-368 monotherapy resulted in 74% tumor growth inhibition and anti-PD-L1 resulted in complete tumor regression in 2/8 mice. Robust synergy was observed with the combination of ACR-368 and anti-PD-L1, which led to complete tumor regression in 7/8 mice (Part I), and generated durable immune memory persisting beyond 200 days after four sequential tumor re-challenges (Part II-V). Systematic depletion of immune cell subpopulations (Parts III–V) showed that the absence of either CD4+ or CD8+ T-cells alone did not lead to tumor growth upon rechallenge, while co-depletion of both resulted in tumor formation, indicating that immune memory is driven by adaptive immune responses. (B) The combination of ACR-368 and anti-PD-L1 was well tolerated, consistent with non-overlapping toxicities.

ACR-368 activates ssDNA/dRNA sensing and innate immune signaling pathways

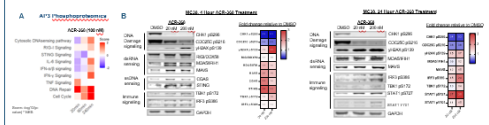


Figure 2: Activation of innate immune signaling and nucleic acid sensing pathways *in vitro*. (A) Acrivon Predictive Precision Proteomics (AP3) analysis of MC38 cells showed a time-dependent increase in phosphorylation of proteins associated with multiple innate immune signaling and DNA damage pathways after ACR-368 treatment vs DMSO. (B) Western blot analysis of selected markers in ACR-368 treated cells (20nM, 200nM) showed reduction in CHK1 activity accompanied by an increase in DNA damage, ssDNA/dsRNA sensing (4h), and subsequent activation of innate immunity pathways (24h).

ACR-368 activates DNA damage responses and induces apoptotic cell death *in vivo*

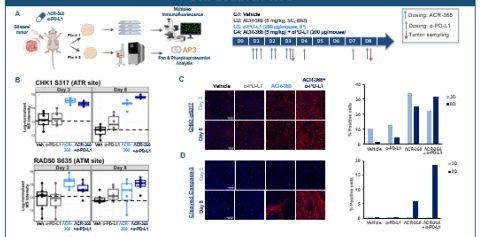


Figure 3: Robust induction of DNA damage response signaling by ACR-368 *in vivo*. (A) Mice with bilateral syngeneic tumors were treated with vehicle, ACR-368 (5 mg/kg), anti-PD-L1 (200 µg/mouse), or the combination. Tumors from either flank were collected for immunostaining (IF) or AP3 profiling. AP3 analysis confirms drug activity as indicated by the strong induction of ATM (RAD50-S635) and ATR (CHK1-S317) –phosphorylation sites at early and late timepoints (lower panels). (C) Spatial IF analysis of Day 3 and Day 8 samples confirms ACR-368 driven ATR activation and subsequent apoptosis in Day 8, as indicated by cleaved caspase-3 staining (D).

Enhanced innate immune signaling and modulation of immune pathways by ACR-368 and anti-PD-L1 combination

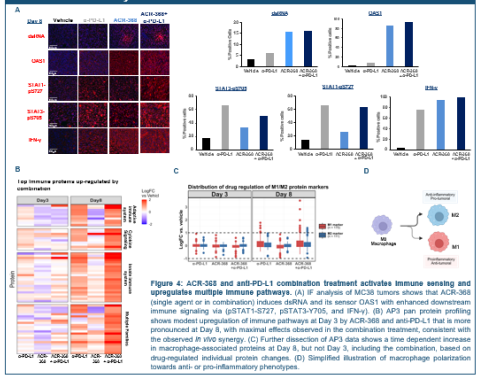


Figure 4: ACR-368 and anti-PD-L1 combination treatment activates immune sensing and upregulates multiple immune pathways. (A) IF analysis of MC38 tumors shows that ACR-368 (single agent or in combination) induces dsRNA and its sensor OAS1 with enhanced downstream immune signaling via (pSTAT1-S727, pSTAT3-Y705, and IFN-γ). (B) AP3 pan protein profiling shows modest upregulation of immune pathways at Day 3 by ACR-368 and anti-PD-L1 that is more pronounced at Day 8, with maximal effects observed in the combination treatment, consistent with the observed *in vivo* synergy. (C) Further dissection of AP3 data shows a time dependent increase in macrophage-associated proteins at Day 8, but not Day 3, including the combination, based on drug-regulated individual protein changes. (D) Simplified illustration of macrophage polarization towards anti- or pro-inflammatory phenotypes.

ACR-368 in combination with anti-PD-L1 promotes pro-inflammatory macrophage phenotypes and enhances cytotoxic innate and adaptive immune responses

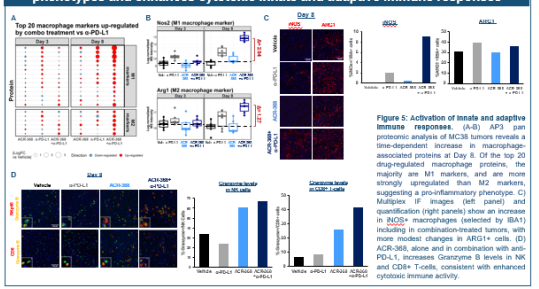


Figure 5: Activation of Innate and adaptive immune responses. (A-B) AP3 pan proteomic analysis of MC38 tumors reveals a time-dependent increase in macrophage-associated proteins at Day 8. Of the top 20 drug-regulated macrophage proteins, the majority are M1 markers, and are more strongly upregulated than M2 markers, suggesting a pro-inflammatory phenotype. C) Multiplex IF images (left panel) and quantification (right panels) show an increase in INOS+ macrophages (selected by IBA1) including in combination-treated tumors, with more modest changes in ARG1+ cells. (D) ACR-368, alone and in combination with anti-PD-L1, increases Granzyme B levels in NK and CD8+ T-cells, consistent with enhanced cytotoxic immune activity.

ACR-368 is associated with reduced T-cell exhaustion marker expression in combination with anti-PD-L1

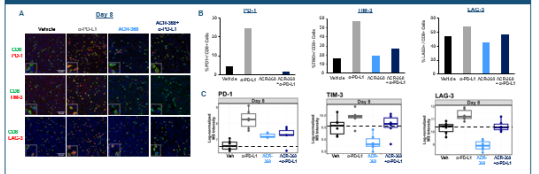
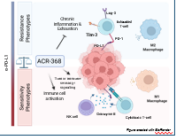


Figure 6: Suppression of T-cell exhaustion markers by ACR-368. (A) Multiplex IF analysis of MC38 tumors at Day 8 shows expression of PD-1, TIM-3, and LAG-3 across treatment groups. (B-C) IF quantifications (upper panels) and AP3 proteomic analysis (lower panels) demonstrate that anti-PD-L1 treatment is associated with increased exhaustion marker expression, while ACR-368, alone and in combination, is associated with lower levels of PD-1, TIM-3, and LAG-3.

Conclusions

- ACR-368 activates the DNA damage response accompanied by robust innate immune signaling in MC38 cells *in vitro* and *in vivo*.
- AP3 pan- and phospho-proteomics coupled with spatial IF immune profiling demonstrate activation of both the innate and adaptive components of the immune system, together with suppression of T-cell exhaustion markers.
- ACR-368 combined with anti-PD-L1 provides a balanced, sustainable inflammatory response leading to anti-tumor efficacy and long-term immune memory.
- These data provide a strong mechanistic rationale for clinical evaluation of ACR-368 in combination with ICIs to enhance the clinical efficacy of these agents.



AACR 2026: ACR-368 SYNERGY WITH TOPOISOMERASE I

Poster # 239

Potent Synergy Between CHK1/2 Inhibitor ACR-368 and the ADC Payload Topoisomerase I Inhibitor: Rationale for ADC + ACR-368 Combination Therapy

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[1]Acrivon Therapeutics Inc., Watertown MA, USA; [2]Acrivon AB, Medicon Village, Lund, Sweden; *Authors contributed equally

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Introduction

- Antibody-drug conjugates (ADCs) enable targeted delivery of cytotoxic payloads to tumor cells, improving the therapeutic index compared with conventional chemotherapy. Topoisomerase I (Topo I) inhibitors are potent ADC payloads that trap the Topo I-DNA cleavage complex, leading to replication-fork collapse and tumor cell death. However, this also activates the DNA damage response through CHK1/2-dependent cell cycle checkpoints, attenuating cytotoxicity and enhancing resistance to Topo I-containing ADCs.
- CHK1/2 inhibition exploits this therapeutic vulnerability, abrogating these checkpoints, increasing replication stress, and thereby enhancing the efficacy of Topo I inhibitors across multiple tumor models. Consistent with this, treatment with the potent, selective CHK1/2 inhibitor ACR-368 (preexacerbib) combined with irinotecan has demonstrated encouraging clinical activity in heavily pretreated patients with sarcomas who had progressed on prior irinotecan therapy.[1] Taken together, these data provide a strong rationale for combining ACR-368 with Topo I inhibitor–based therapies.
- Using the Acrivon Predictive Precision Proteomics (AP3) platform, we previously identified endometrial cancer as a tumor type predicted to be particularly sensitive to ACR-368, which has been shown and is being further evaluated in a Phase 2 registrational trial.
- In a panel of endometrial cancer cell lines, the combination of ACR-368 with exatecan or SN38 demonstrated synergy in a majority of these, with comparable synergy scores between both Topo I inhibitors. Pathway mechanisms underlying Topo I inhibitor sensitivity and resistance and the potent, synergistic activity with ACR-368 were identified using AP3 Generative Phosphoproteomics.

AP3 Identifies Mechanisms of Topoisomerase I Inhibitor Sensitivity

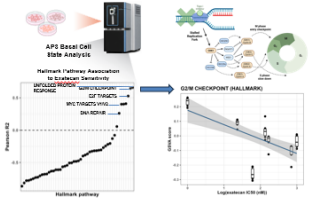


Fig 1. AP3 identifies G2/M Checkpoint Pathway Association With increased Sensitivity to Topo I Inhibition and Rationale for CHK1/2 Inhibition with ACR-368. Pearson correlation of baseline phosphoproteomics-derived Hallmark pathway enrichment scores with Topo I inhibitor (exatecan) IC_{50} values across eight human endometrial cancer cell lines. IC_{50} values were determined by 3-day CellTiter-Glo (CTG) assays (see Fig. 2A). Pathway schematic (top right) highlights G2/M checkpoint regulation downstream of CHK1.[2]

ACR-368 Combines Synergistically with Topo I Inhibitors Across Sensitive and Insensitive Endometrial Models

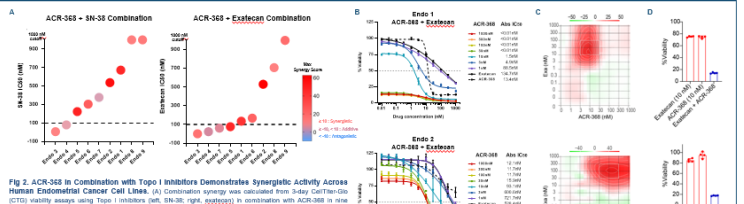


Fig 2. ACR-368 In Combination with Topo I Inhibitors Demonstrates Synergistic Activity Across Human Endometrial Cancer Cell Lines. (A) Combination synergy was calculated from 3-day CellTiter-Glo (CTG) viability assays using Topo I inhibitors (left, SN-38; right, exatecan) in combination with ACR-368 in nine human endometrial cancer cell lines (Endo 1-9). Maximum (max) synergy score was calculated using SynergyFinder and indicated by bubble color; cell lines were ranked (x-axis) by Topo I inhibitor IC_{50} values (1000 nM cutoff used for values ≥ 1000 nM); dashed line denotes 100 nM IC_{50}. (B-C) Plots shown for Endo 1 (above) and Endo 2 (below) cell lines. (B) Representative 3-day CTG viability curves for ACR-368 + exatecan in selected cell lines. (C) Bliss synergy plots with corresponding maximum synergy scores calculated using SynergyFinder. (D) Selected dose combinations from (B) demonstrate enhanced loss of viability with ACR-368 + exatecan (blue) relative to single agents.

AP3 Reveals Exatecan-Mediated Suppression of Cell Cycle Programs, Relieved by ACR-368

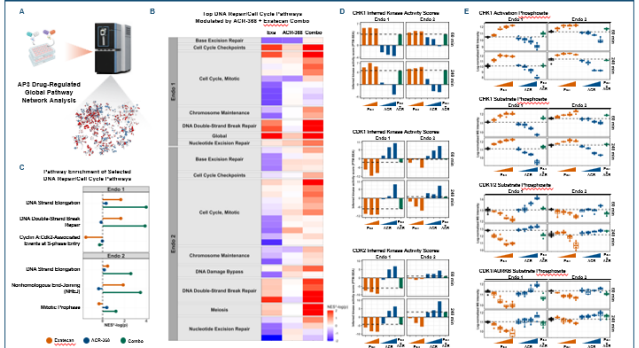


Fig 3. ACR-368 Uncouples Cell Cycle Control from Exatecan-Induced DNA Damage. (A) AP3 pathway analysis reveals global networks of biological pathways in response to drug treatment. (B) Heatmap of normalized enrichment scores (NES) for DNA repair-related pathways from the Reactome database following 60 min drug treatment (10 nM ACR-368, 10 nM exatecan, and their combination) in Endo 1 and Endo 2 cells. Pathways shown are those that exhibited a significant difference in enrichment in the combination treatment compared with single-agent treatment. (C) Pathway enrichment scores of select cell cycle/DNA repair pathways showing differential modulation by treatment as in (B). (D) Inferred kinase activity scores calculated from phosphorylation levels of annotated substrates from the PSP and IKIP databases in Endo 1 and Endo 2 cells after 60 and 240 minutes of single drug treatment (10, 30, 100 nM) or combination (10 nM ACR-368 + 10 nM exatecan). Bars represent the PTM-SEA scores of inferred kinase activities; positive scores indicate increased activity relative to DMSO control and negative values indicate decreased activity. Dashed line indicates the inferred activity level post-combination treatment. (E) Log-normalized phospho-peptide abundance; points represent individual replicate measurements, lines indicate the median across replicates at each dose (1, 10, 30, 100 nM exatecan; 3, 10, 30, 100 nM ACR-368) and in combination (10 nM ACR-368 + 10 nM exatecan). Boxes represent the interquartile range. Dashed horizontal line denotes the DMSO (-) control level for each condition.

ACR-368-Mediated Checkpoint Release Drives Replication Catastrophe with Topo I Inhibitor

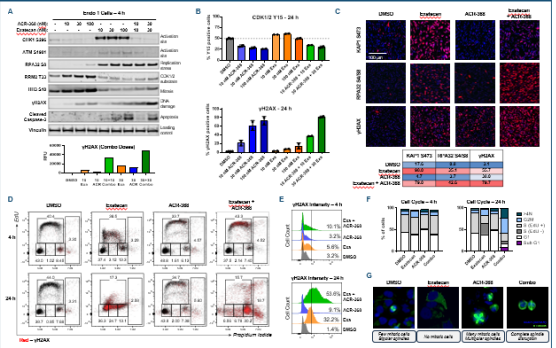


Fig 4. ACR-368 Suppresses the CHK1/2 Checkpoint Response induced by Exatecan, to Enhance Cell Death by Replication Catastrophe and Mitotic Collapse. (A) Above, Western blot validation of selected cell cycle DNA repair pathway members after 4h treatment with ACR-368 (ACR) and exatecan in Endo 1 cells; below, quantification of γH2AX signal (combination doses shown). (B) CDK1/2 Y15 (above) and γH2AX (below) levels after 24h of treatment with ACR-368, exatecan, or the combination, measured by immunofluorescence and quantified relative to DMSO control. (C) Immunofluorescence staining of cell pellets prepared from Endo 1 cells treated for 4 hours with 30 nM exatecan, 30 nM ACR-368, or the combination. Quantification of staining, shown below, was performed using HALO® software. (D-F) Endo 1 cells treated with 10 nM exatecan, 10 nM ACR-368, or in combination for 4 h (top) or 24 h (bottom). Cell cycle distribution was evaluated by flow cytometry using propidium iodide (PI) and EdU incorporation, with γH2AX high cells (red) overlaid on the cell-cycle profiles (D); histograms of γH2AX intensity (E); and quantification of cell cycle distribution (F). (G) Representative images from Endo 1 cells treated for 24 h with 30 nM exatecan, 30 nM ACR-368, or the combination, captured at 20X on a CX5 high content imager (Blue: nuclei, Hoechst stain; Green: α-tubulin).

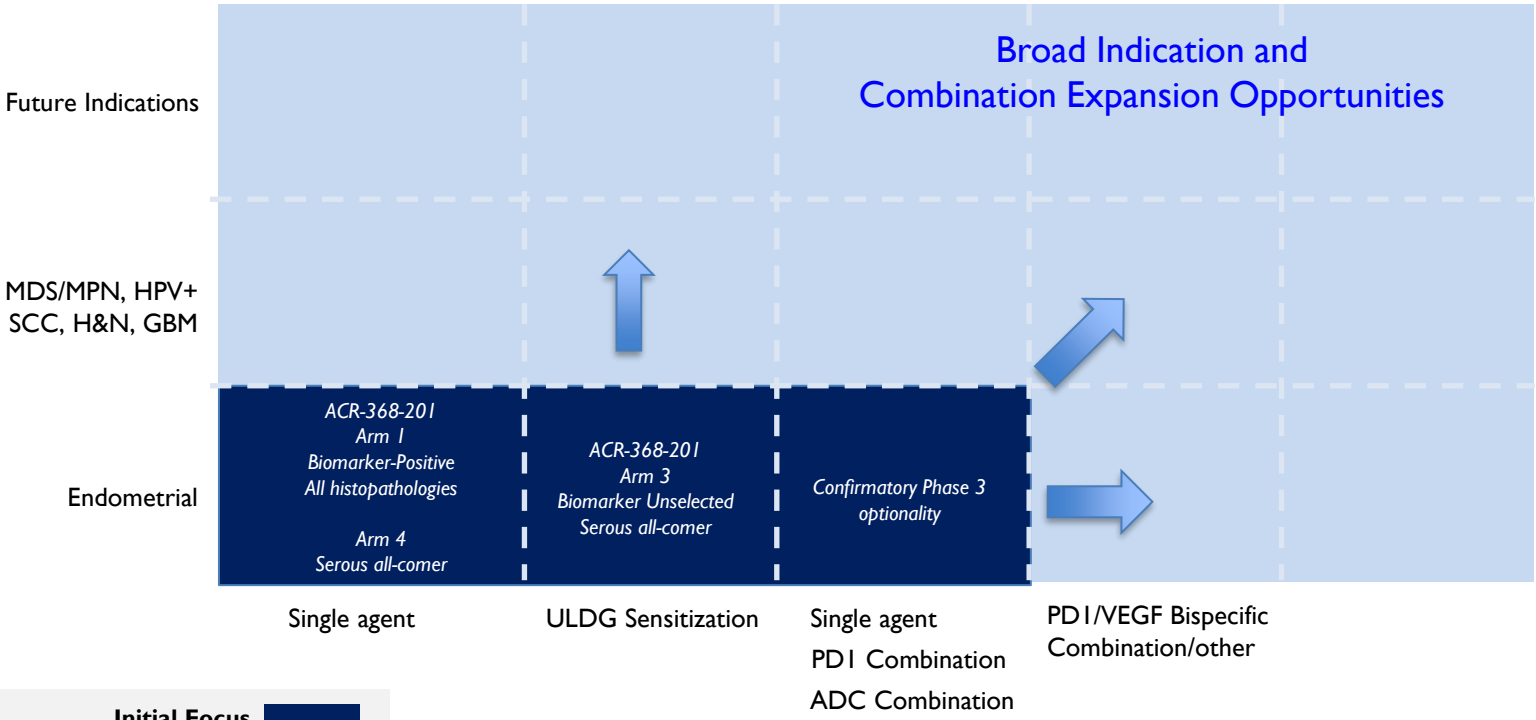
Conclusions



- AP3 Generative Phosphoproteomics identified modulation of the G2/M checkpoint pathway as associated with increased sensitivity to Topo I inhibition, providing a mechanistic rationale for combination with ACR-368, a first-in-class CHK1/2 inhibitor currently in an ongoing registrational intent Phase 2b study in endometrial cancer, that enhances G2/M pathway activation through checkpoint inhibition.
- ACR-368 demonstrated synergistic activity with Topo I inhibitors in both Topo I inhibitor–sensitive and –insensitive models, supporting the potential to overcome resistance to Topo I inhibitor–based ADCs.
- Phosphosite and kinase activity signatures identified by AP3 implicated replication stress response and checkpoint inhibition as key mechanisms underlying the synergistic cell death observed with the combination.
- Synergy was observed at low doses of both agents, suggesting the potential for dose reduction while maintaining antitumor activity, which may provide opportunity to move ACR-368 toward frontline settings in combination with Topo I inhibitor-payload ADCs.

References:
[1] Bolkin et al. *JCO Oncol Adv* (2025)
[2] Diagram modified from Gorecki, Andis & Korabecny. Cancers (2021), and di Rora et al. *J Hematol Oncol* (2020)
Pathway diagrams / figure icons created with use of BioRender.com

ACR-368 OFFERS MULTIPLE ATTRACTIVE OPPORTUNITIES



INTERNAL PIPELINE: AP3-BASED DRUG DISCOVERY
POTENTIAL FIRST- AND BEST IN CLASS CANDIDATES

ACR-2316: Clinical stage, novel WEE1/PKMYT1 inhibitor

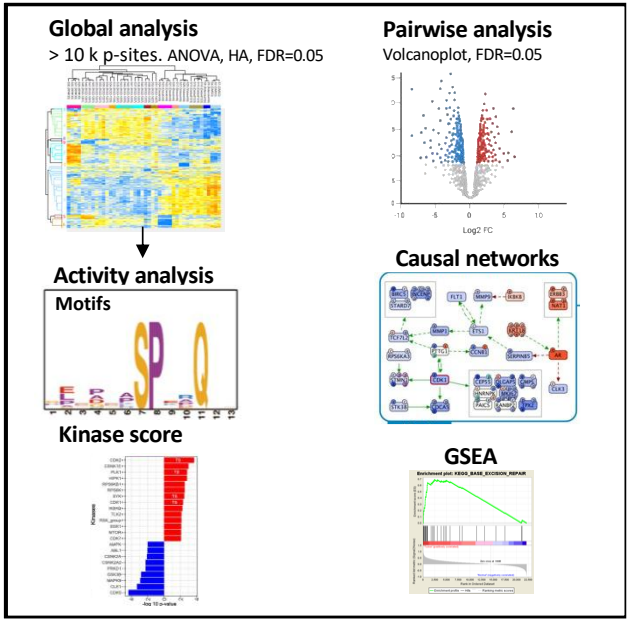
- Additional clinical data and transition to dose expansion 2026

Development candidate, novel CDK11 inhibitor

- Anticipated IND filing 1H 2027
- Multiple equally promising back-up series being pursued in parallel

Additional AP3-based internal programs

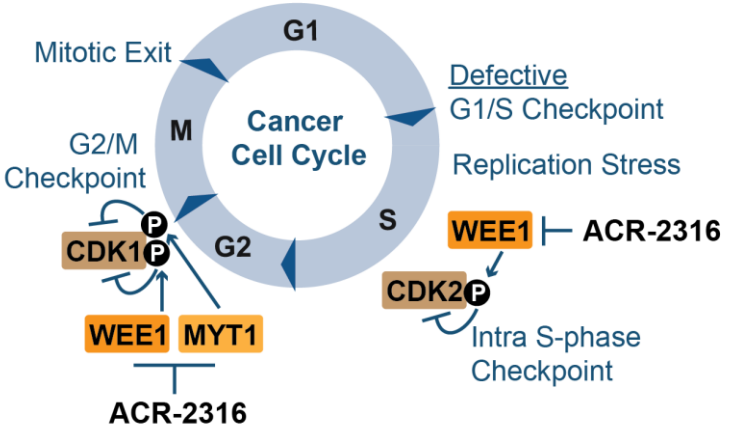
Streamlined AP3-based drug discovery



AP3 used for biologically relevant selectivity profiling

WEE1 AND PKMYT1 - CRITICAL CELL CYCLE CHECKPOINTS IN HUMAN CANCER

- WEE1 and PKMYT1 regulate S and G2-M cell cycle checkpoints to ensure proper DNA replication and mitotic completion
- Defective DNA repair is highly prevalent in cancers, creating a dependency on checkpoint proteins
- Demonstrated clinical activity, but the Therapeutic Index has been challenging
- AP3 was applied to design a molecule with potent single agent activity and exquisite selectivity to achieve expanded Therapeutic Index



ACR-2316 IS A POTENTIALLY BEST- AND FIRST-IN-CLASS AGENT – FIRST POC FOR AP3 PLATFORM

Program Goals		Demonstrated Results
1	Superior single agent activity	▪ Superior anti-tumor activity* (robust CDK1, CDK2, and PLK1 activation; inhibition of PKMYT1 resistance)
2	High selectivity and potency	▪ 5-20-fold more potent* in preclinical models than clinical benchmarks; complete tumor regression
3	Favorable ADME-PK, Therapeutic Index, and tolerability profile	▪ Potent tumor cell killing*, short elim. $T_{1/2}$; only transient AEs ▪ Broad preclinical T.I. and complete tumor regression
4	Streamlined clinical development	▪ Advanced from lead to oral dosing in clinic in ≤15 month ▪ AP3-based Indication Finding ▪ AP3 MS-based PD assay developed for human PBMCs ▪ Two weekly oral dosing regimens established ▪ Durable clinical activity in AP3-predicted tumor types, including SCLC, sqNSCLC ▪ Favorable, differentiated safety, primarily only neutropenia

AP3-Enabled SAR

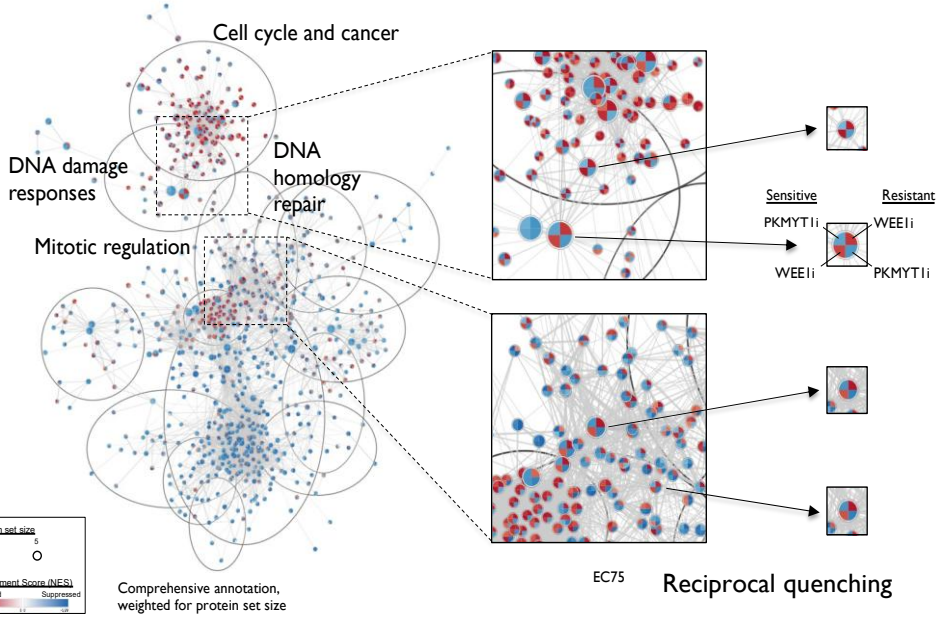
*Head-to-head preclinical studies against benchmarks with clinical data

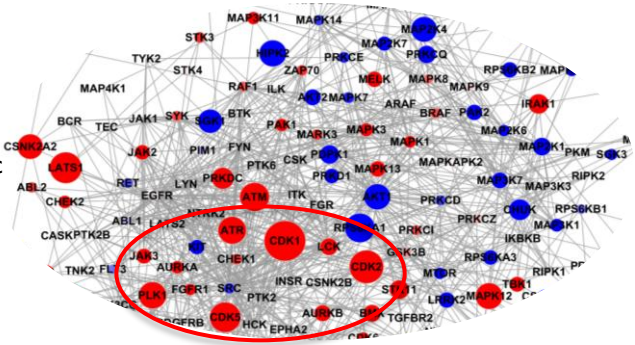
ACR-2316: UNIQUELY DESIGNED BY AP3 FOR SUPERIOR THERAPEUTIC INDEX OVER WEE1 AND PKMYT1 INHIBITORS

ACR-2316: Novel WEE1/PKMYT1 inhibitor with potent single agent activity

- ✓ Complete tumor regression across all models
- ✓ High selectivity (co-crystallography) and short elimination T1/2 to ensure transient, mild AEs
- ✓ Potent WEE1 inhibition, balanced PKMYT1 inhibition, overcomes resistance and enables robust activation of CDK1, CDK2, and PLK1 for mitotic catastrophe
- ✓ Clinical activity observed in AP3-predicted tumor types, including SCLC, SqNSCLC and adenoNSCLC

Drug Design by AP3-based SAR for desirable pathway effects and suppressing resistance mechanisms

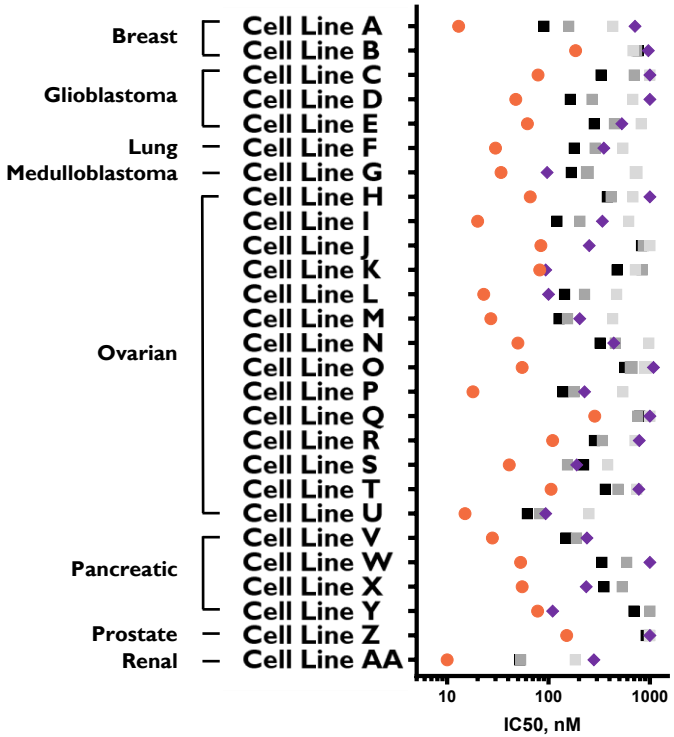


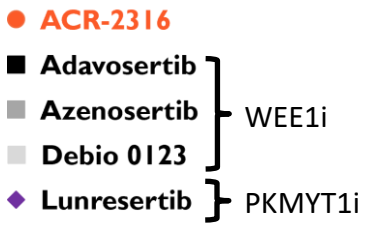


Potent mitotic catastrophe

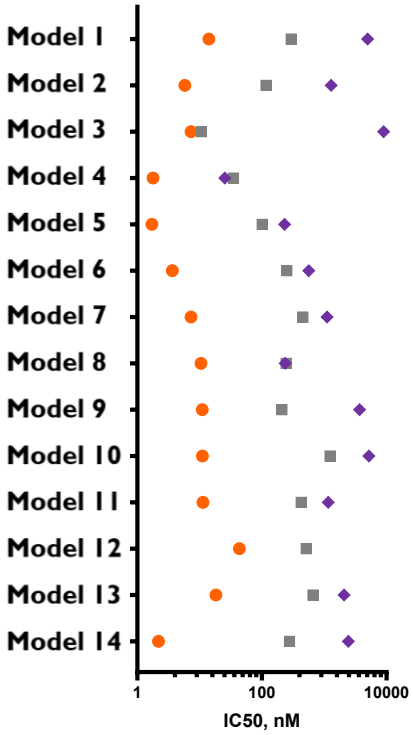
ACR-2316 IS HIGHLY POTENT ACROSS HUMAN TUMOR CELL LINES AND PATIENT-DERIVED *EX VIVO* TUMOR MODELS

Human tumor cell lines (not genetically selected)

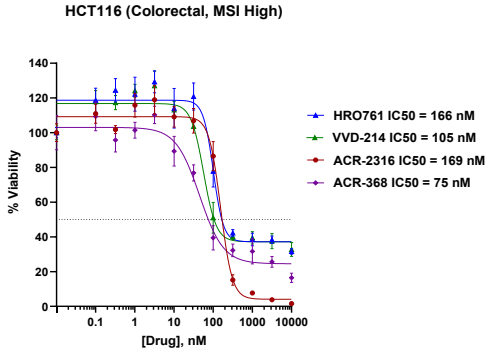


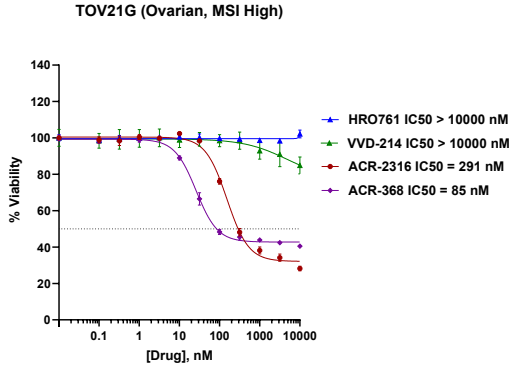


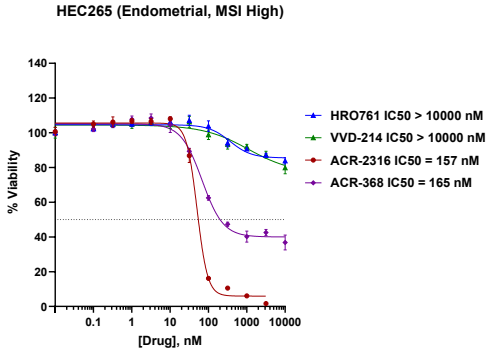
Patient-derived *ex vivo* ovarian tumor models

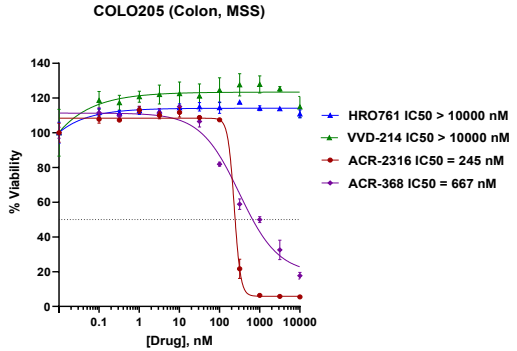


SUPERIOR ACTIVITY OF ACR-2316 OVER WRN INHIBITORS IN BOTH MSI HIGH AND MSS CELL LINES



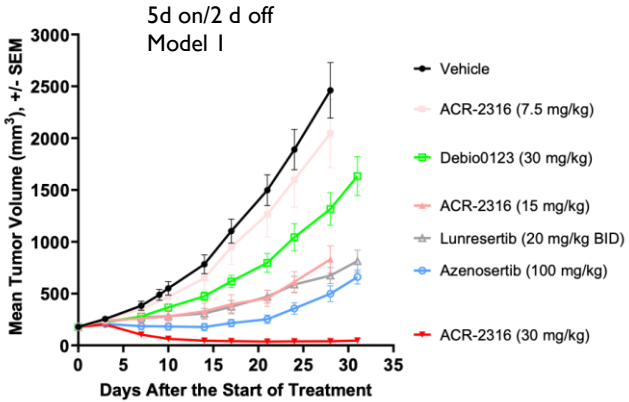


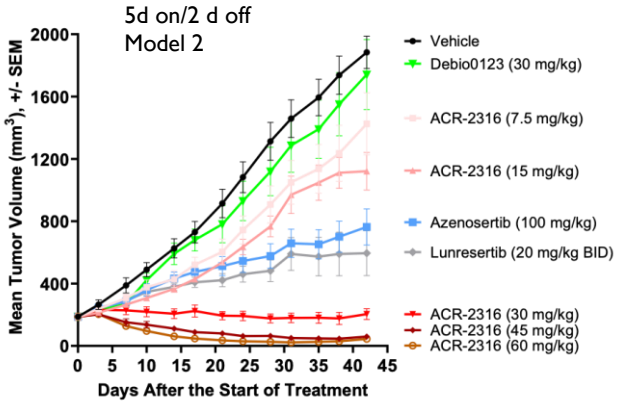


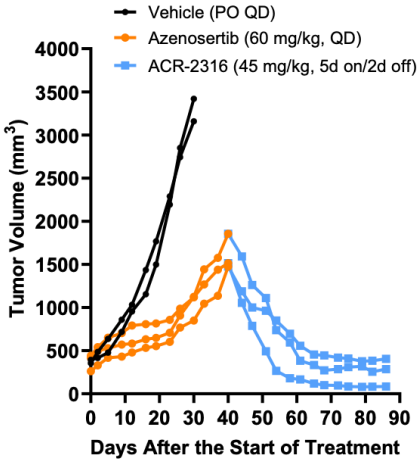


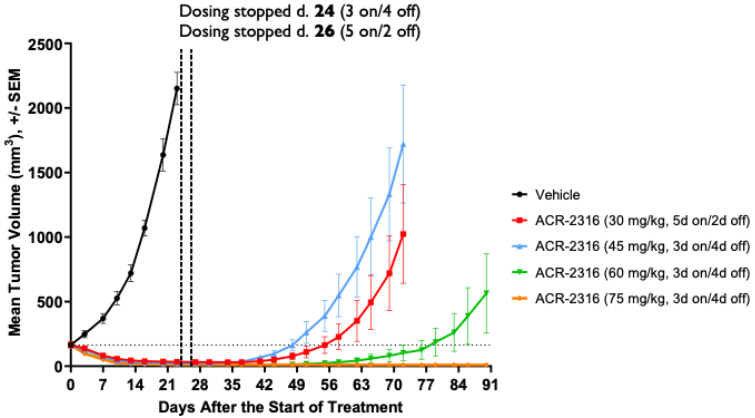
HRO761 is a noncovalent allosteric inhibitor of WRN (Novartis); VVD-133214/ RO7589831 is a covalent allosteric WRN inhibitor (Roche); ACR-2316 is more potent than both WRN inhibitors even in the optimal MSI high context, associated with strong dependency on WRN activity

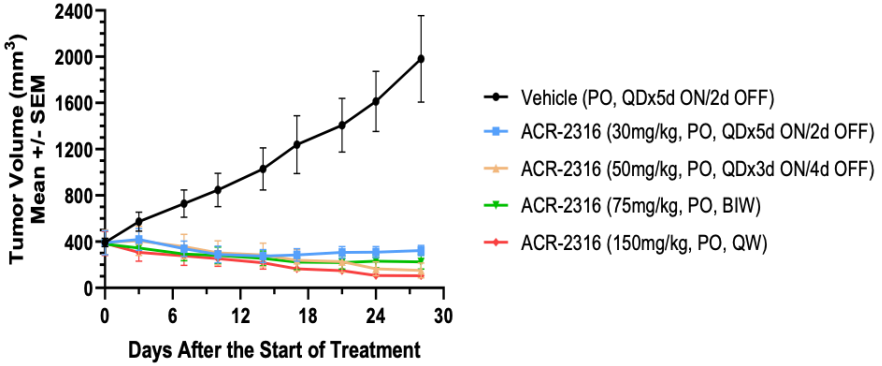
ACR-2316 INDUCES COMPLETE TUMOR REGRESSION ACROSS MODELS AND DOSING REGIMENS







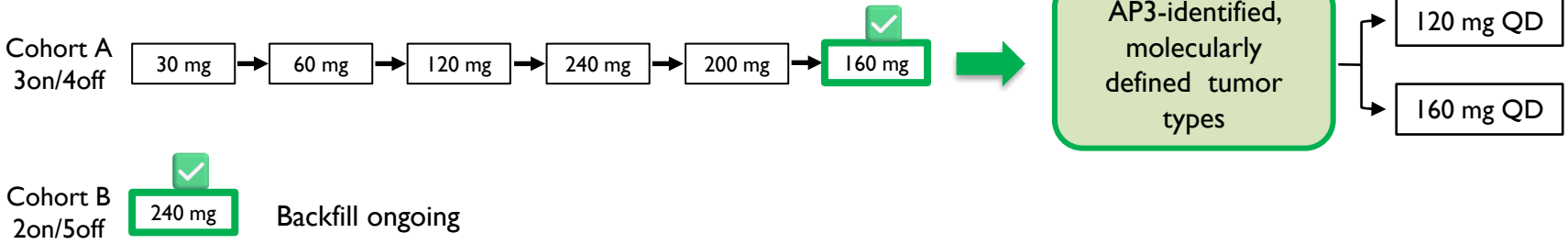




ACR-2316 DOSE EXPANSION IN AP3-DEFINED TUMOR TYPES

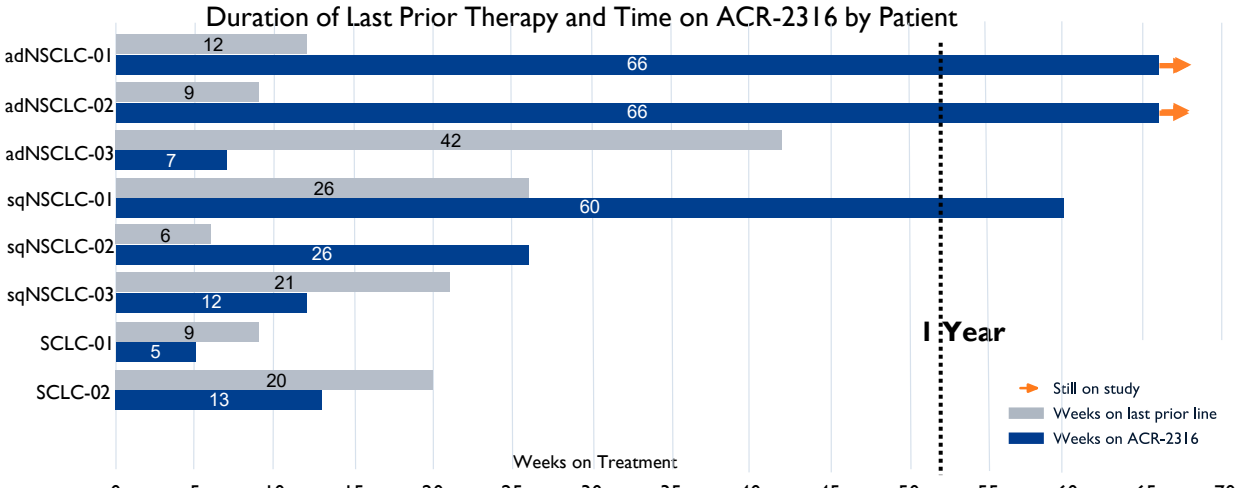
Dose Escalation – 2 weekly oral regimens established (N = 35)

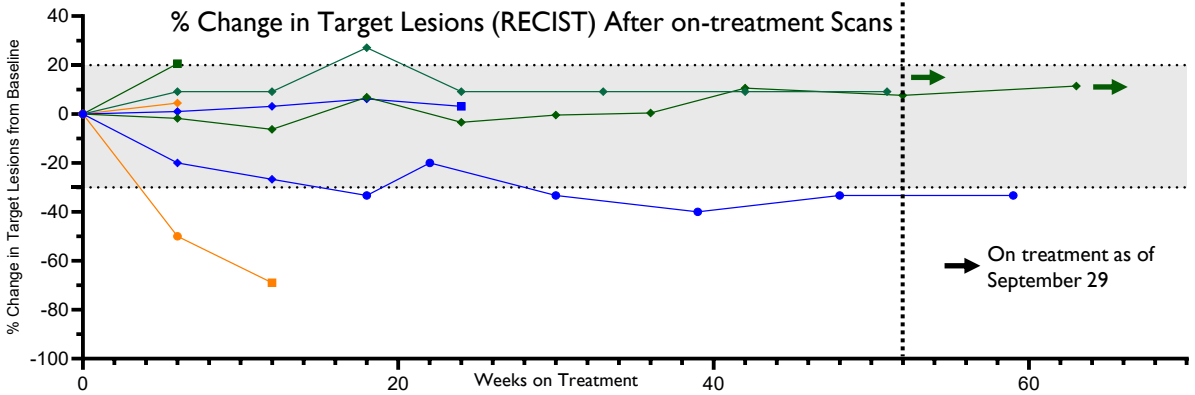
Randomized Dose Expansion: 3d on / 4d off



- Favorable differentiated safety profile, mainly transient heme AEs (predominantly neutropenia)
- Durable clinical activity observed during dose escalation, including in heavily pretreated lung cancer subjects
- Stratification into molecularly defined lung vs non-lung cancer types with 1:1 randomization into 2 dose levels

ACR-2316 DEMONSTRATES CLINICAL ACTIVITY IN HEAVILY PRETREATED LUNG CANCER PATIENTS





- Durable single-agent activity, including tumor shrinkage and PRs
- Clinical benefit over 1 year in several heavily pretreated subjects (median 3 prior lines, including ICI and chemo)

Non QC'd data based on EDC as of 9/29/2026

DIFFERENTIATED, FAVORABLE SAFETY PROFILE, PRIMARILY LIMITED TO TRANSIENT NEUTROPENIA

Established weekly dosing regimens; N = 22

Event	Grade 3 n (%)	Grade 4 n (%)	Grade ≥3 n (%)
Neutropenia	4 (18.2)	2 (9.1)	6 (27.3)
Leukopenia	1 (4.5)	1 (4.5)	2 (9.1)
TOTAL (unique subjects)	**5 (22.7)**	**2 (9.1)**	**6 (27.3)**

Grade ≥3 treatment-related AEs with incidence ≥5% shown; no Grade 5 TRAEs.
TOTAL: Subjects counted individually in Grade 3 and Grade 4 columns; same subject counted only once in Grade ≥3 column

- **Primarily transient, mechanism-based hematological AEs, mainly neutropenia**
- **No other types of toxicities observed above (N = 13) tolerated weekly doses**
- **Notable absence of GI toxicities, long-lasting myelosuppression or more severe non-hematological AEs commonly seen with ADCs and chemotherapy**

Non QC'd data based on EDC as of 7/31/2026

ACR-2316-101 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Subject Demographics	N = 35
Median Age, years (range)	63.0 (35–77)
Sex, n (%)	
Female	22 (62.9)
Male	13 (37.1)
Race, n (%)	
White	27 (77.1)
Black/African American	4 (11.4)
Asian	1 (2.9)
Native Hawaiian/Pacific Islander	1 (2.9)
Other/Unknown/Not Reported	2 (5.7)

Cancer Type, n (%)	N = 35
Endometrial	6 (17.1)
Ovarian Carcinoma	5 (14.3)
Breast	4 (11.4)
Adenocarcinoma NSCLC	3 (8.6)
Colorectal	3 (8.6)
Head & Neck SCC	3 (8.6)
Squamous NSCLC	3 (8.6)
Pancreatic	2 (5.7)
Prostate (Neuroendocrine)	2 (5.7)
Small Cell Lung Cancer	2 (5.7)
Bladder	1 (2.9)
Cervical	1 (2.9)

ECOG Status at Baseline, n (%)	
0	11 (31.4)
1	24 (68.6)
Prior Lines of Therapy, n (%)	
1	1 (2.9)
2	5 (14.3)
3	16 (45.7)
4	7 (20.0)
5	1 (2.9)
≥6*	5 (14.3)*

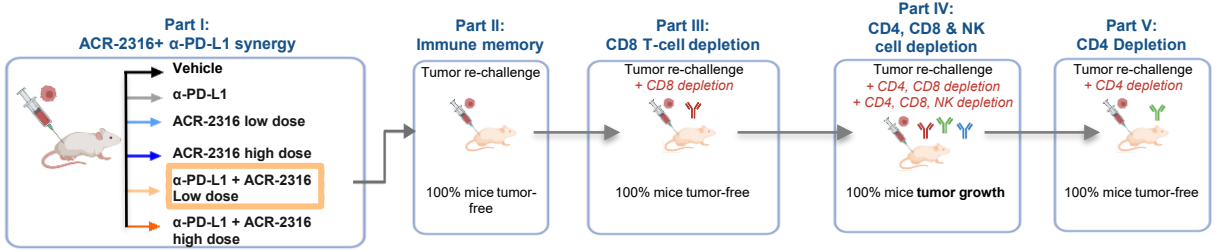
* ≥6 prior lines: 3 with 6; 1 with 7; 1 with 8

Prior Exposure to IO Therapy, n (%)	
Yes	26 (74.3)
No	9 (25.7)

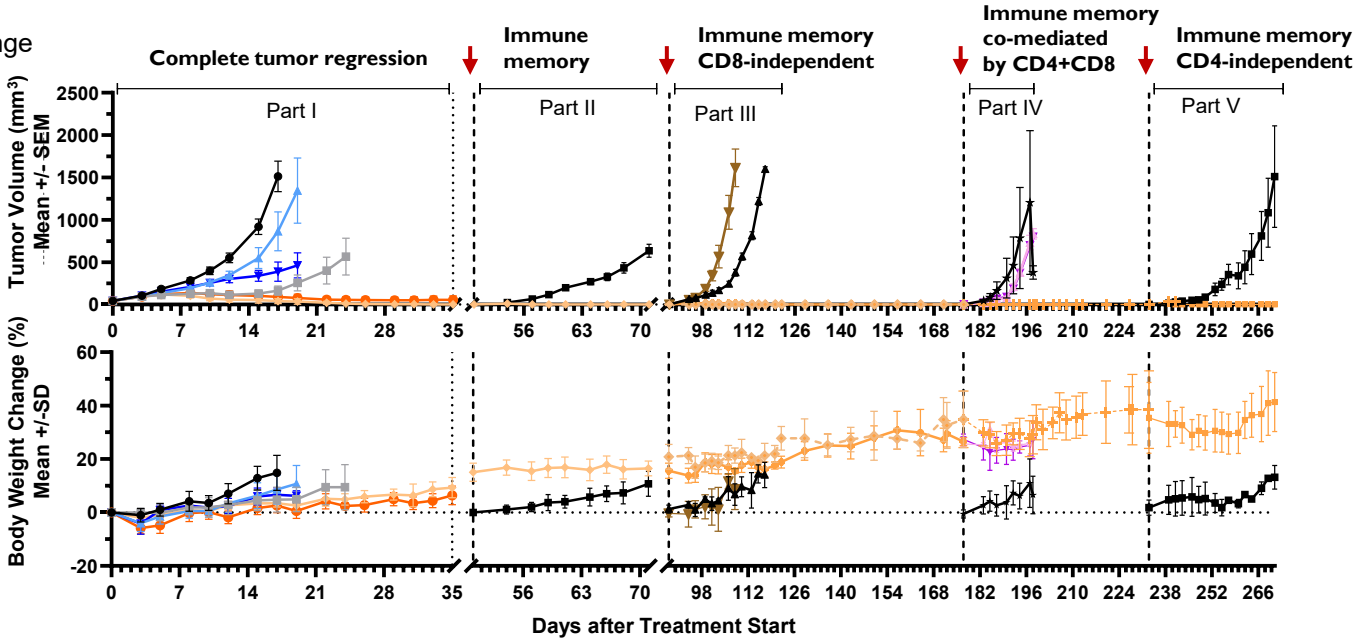
NSCLC = non-small cell lung cancer.
SCC = squamous cell carcinoma.

Non QC'd data based on EDC as of 07/31/2026

POTENT ACR-2316 + ANTI-PD-L1 SYNERGY WITH COMPLETE TUMOR REGRESSION AND IMMUNE MEMORY MEDIATED BY CD4+ AND CD8+ CELLS



Tumor cell re-challenge



AACR 2026: ACR-2316 SYNERGY WITH CHECKPOINT INHIBITION

Poster # 3789

Treatment with ACR-2316, a potential first- and best-in-class WEE1/PKMYT1 inhibitor, combined with anti-PD-L1 induces complete tumor regression with durable immune memory in a preclinical syngeneic model

Taronish Dubash[1], Joelle Baddour-Sousounis[1], Amira Elbakry[1], Jessica Hopkins[1], Subodh Kumar[1], Yingchun Spring Liu[1], Ahmed Youssef[1], Kate Rappard[1], Ignacio Arribas Diez[2], Georgia Mitsa[2], Marc Isaksson[2], Francisco Santana[1], Maria Rodriguez-Zabala[1], Luka Romero[1], Zachary Best[1], Nina Lipjankic[2], Anna-Maria Alves[1], Daphne García-Lopez[1], Portia Lombardo[1], Calvin Yang[1], Emma Ahrman[2], Valentina Siino[2], Reina Improgo[1], Magnus E. Jakobsson[2], Helen Nilsson[2], Ayesha Murshid[1], Lei Shi[1], Caroline Wigerup[2], Michail Shipitsin[1], Joon Jung[1], David Proia[1], Erick Gamelin[1], Kristina Masson[1], Peter Blume-Jensen[1]

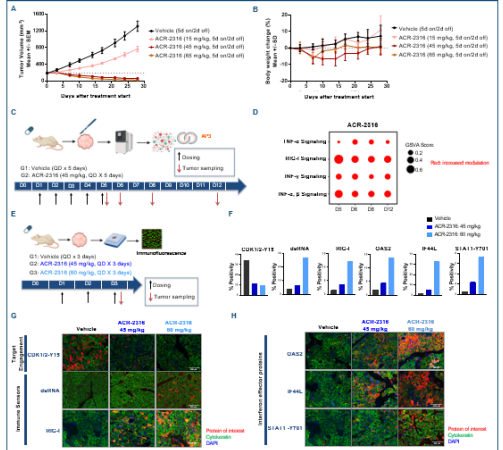
[1]Acrivon Therapeutics Inc., Watertown MA, USA; [2]Acrivon AB, Medicon Village, Lund, Sweden

Acrivon Therapeutics
Website: Acrivon.com
Contact: Partnerships@Acrivon.com

Introduction

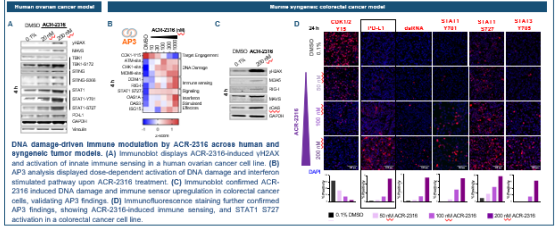
- WEE1 and PKMYT1 have critical roles in the S and G2/M checkpoint and replication stress response. ACR-2316 is a potent WEE1/PKMYT1 inhibitor designed by Acrivon's Predictive Precision Proteomics (AP3) for superior pro-apoptotic tumor cell killing through balanced inhibition of PKMYT1, uncovered by AP3 as a dominant resistance mechanism to WEE1 inhibition, resulting in potent activation of not only CDK1 and 2, but importantly also PLK-1.
- Based on this mechanism, ACR-2316 is expected to exacerbate tumor-intrinsic DNA damage and induce strong mitotic catastrophe in genetically unstable cancers, resulting in activation of innate immune sensing pathways, providing a mechanistic link between replication stress and adaptive anti-tumor immunity.
- Here, we evaluated ACR-2316 in human and murine syngeneic cancer models to characterize its effects on DNA damage response signaling and immune activation. We further assessed combination with anti-PD-L1 to determine whether DDR-driven tumor priming enhances tumor regression and induces durable immune memory, and profiled associated signaling using our AP3 platform.

AP3 profiling of ACR-2316-treated tumors reveals activation of innate immune signaling pathways



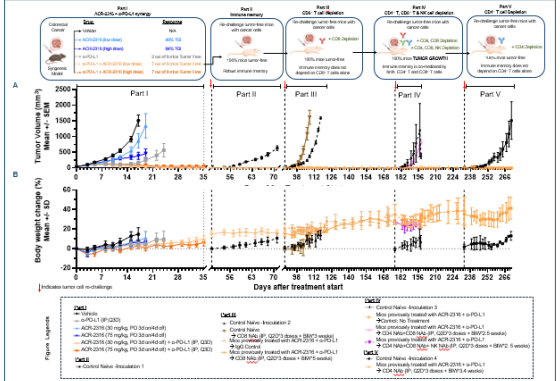
Robust anti-tumor activity and induction of innate immune signaling in human CDX model. (A) In a human ovarian tumor CDX model, ACR-2316 (5d on/2d off dosing) displayed dose-dependent tumor growth inhibition, including tumor regression, and **(B)** was well-tolerated. **(C)** Mice were treated with vehicle or ACR-2316 (45 mg/kg, QD × 5d on), and their tumors were collected at indicated time points for AP3. **(D)** Heatmap of GSVA pathway signature pan proteomic scores from tumor samples collected at 6 hours post-dosing on days 5, 6, 8 and 12 demonstrate increased modulation of innate immune signaling with ACR-2316 treatment. **(E)** Tumor-bearing mice were treated daily for 3 days with vehicle or ACR-2316 (45 or 60 mg/kg, QD × 3d on), and tumors were collected 6 hours post-dosing on day 3 for immunofluorescence analysis. **(F-H)** Representative sections and quantifications show induction of innate immune and interferon response markers.

ACR-2316 induces tumor-intrinsic DNA damage and activates multi-dimensional immune sensing in human and murine syngeneic cancer models



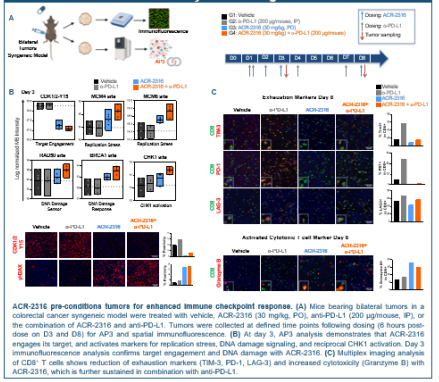
DNA damage-driven immune modulation by ACR-2316 across human and syngeneic tumor models. (A) Immunoblot displays ACR-2316-induced γH2AX and activation of innate immune sensing in a human ovarian cancer cell line. **(B)** AP3 analysis displayed dose-dependent activation of DNA damage and interferon stimulated pathway upon ACR-2316 treatment. **(C)** Immunoblot confirmed ACR-2316 induced DNA damage and immune sensor upregulation in colorectal cancer cells, validating AP3 findings. **(D)** Immunofluorescence staining further confirmed AP3 findings, showing ACR-2316-induced immune sensing, and STAT1 S727 activation in a colorectal cancer cell line.

ACR-2316 synergizes with anti-PD-L1 to induce complete response and durable immune memory in a syngeneic tumor model, co-mediated by CD4⁺ and CD8⁺ T cells



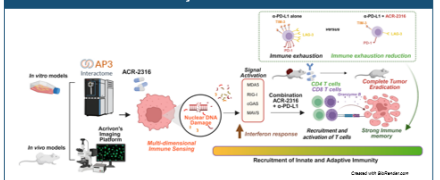
Durable complete tumor regression and long-term immune memory characterization. (A) In a syngeneic colorectal cancer model, ACR-2316 showed dose-dependent tumor growth inhibition as monotherapy. In combination with anti-PD-L1, ACR-2316 exhibited robust synergy, leading to complete tumor regression in 7/8 mice at both tested doses (Part I, treatment stopped at day 35). Previously cured mice remained tumor-free for over 200 days after four sequential re-challenges, demonstrating durable immune memory (Part II). To define the mechanism of durable immunity, key immune cell subsets were depleted during re-challenge (Parts III–V). Depletion of CD4⁺ (Part V) or CD8⁺ (Part III) T cells alone did not restore tumor growth, whereas co-depletion of both subsets (Part IV) led to tumor formation. **(B)** The combination of ACR-2316 and anti-PD-L1 was well-tolerated, consistent with non-overlapping toxicities.

ACR-2316 boosts immune-mediated tumor killing and overcomes anti-PD-L1 resistance by decreasing T-cell exhaustion



ACR-2316 pre-conditions tumors for enhanced immune checkpoint response. (A) Mice bearing bilateral tumors in a colorectal cancer syngeneic model were treated with vehicle, ACR-2316 (30 mg/kg, PO), anti-PD-L1 (200 µg/mouse, IP), or the combination of ACR-2316 and anti-PD-L1. Tumors were collected at defined time points following dosing (6 hours post-dose on D3 and D8) for AP3 and spatial immunofluorescence. **(B)** At day 3, AP3 analysis demonstrates that ACR-2316 engages its target, and activates markers for replication stress, DNA damage signaling, and reciprocal CHK1 activation. Day 3 immunofluorescence analysis confirms target engagement and DNA damage with ACR-2316. **(C)** Multiplex imaging analysis of CD8⁺ T cells shows reduction of exhaustion markers (TIM-3, PD-1, LAG-3) and increased cytotoxicity (Granzyme B) with ACR-2316, which is further sustained in combination with anti-PD-L1.

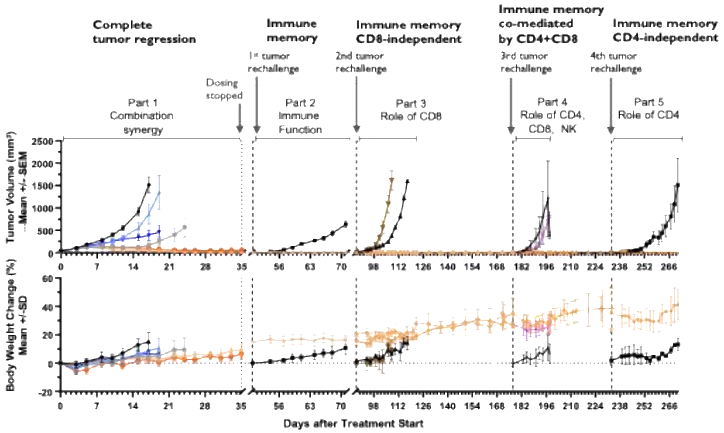
Summary and Conclusions



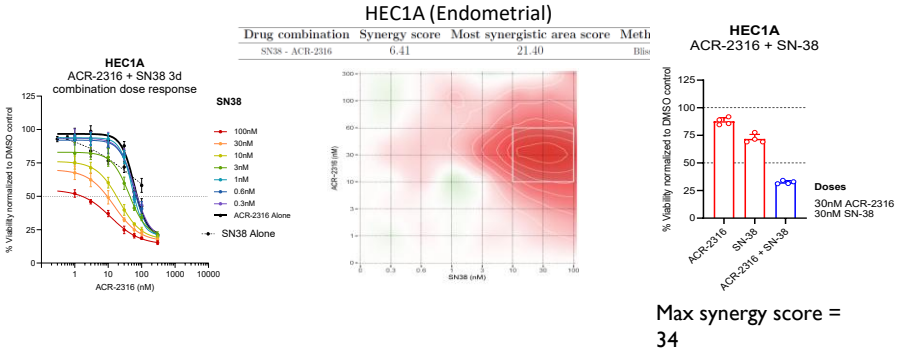
- ACR-2316 induces tumor-intrinsic DNA damage and activates innate immune sensing pathways, including interferon and inflammatory signaling programs.
- In a syngeneic model, ACR-2316 combination with anti-PD-L1 enhances tumor regression and induces durable CD4⁺CD8⁺ T cell-mediated immune memory, supporting coordinated adaptive immunity along with reduction of T cell exhaustion markers.
- These findings suggest that dual WEE1/PKMYT1 inhibition may couple replication stress-driven DNA damage to immune activation, providing a mechanistic rationale for combination with checkpoint blockade.

POTENTIAL DEVELOPMENT PATHS FOR ACR-2316

- AP3-predicted solid tumor types of high unmet need, e.g. SCLC, sqNSCLC, HPV+ tumors, etc., in ≥2nd line
  - Single agent
  - Chemo combination (DDR stress sensitization)
- ACR-2316 (oral) in combination with either anti-PD(L)1 or TOPO1 payload ADCs based on strong synergistic MOA and observed synergy across preclinical models



ACR-2316 + anti-PD-L1 therapy results in complete regression and permanent CD4 + CD8-mediated immune memory

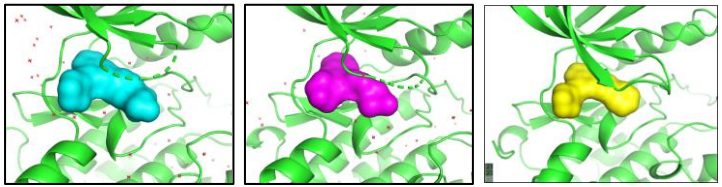


Max synergy score = 34

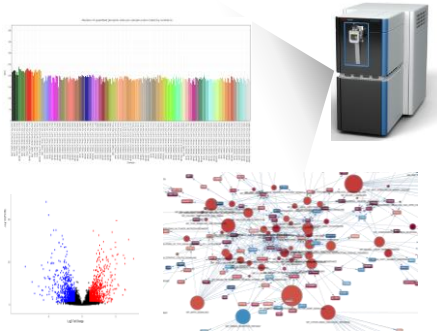
ACR-2316 + TOPO1 payload ADCs show strong synergy in preclinical models

CDK11 PROGRAM HIGHLIGHTS

- **First-in-class opportunity:** No known clinical-stage selective CDK11 inhibitors
- **Compelling oncology target:** Broad role in cell cycle control and oncogenesis, including transcription, pre-mRNA processing and splicing of mitotic genes
- **AP3 fit:** AP3-based cellular SAR and AP3 indication finding identify AML and PTCL as clinical opportunities
- **Multiple development candidates:** Several CDK11 inhibitors being advanced in early IND-enabling studies
  - Highly selective (kinome scan), orally available, potent (single digit nM cellular target engagement; <30 nM EC50 viability), preclinical activity with complete tumor regression



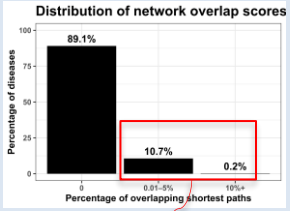
All AP3-driven programs deploy co-crystallography



AP3-based screening funnel guides intracellular protein SAR

AP3-BASED INDICATION FINDING IDENTIFIES AML AS ONE OF THE TOP INDICATIONS FOR CDK11 INHIBITION

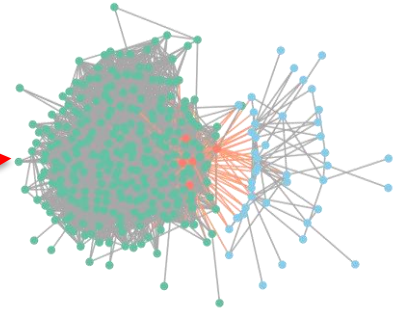
AP3 Indication Screening for CDK11 inhibitor (>2000 diseases)



Top 10 indications matching AP3 profile

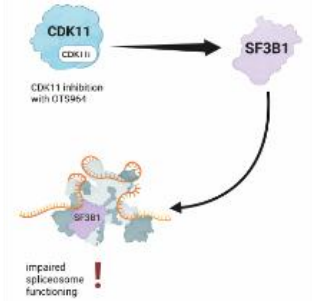
Disease	Classification	Rank
T-cell non-Hodgkin lymphoma	Hematologic	1
Cutaneous T-cell lymphoma	Hematologic	2
Malignant glioma	Solid tumor	3
Peripheral T-cell lymphoma	Hematologic	4
Lysosomal storage disease	Metabolic	5
T-cell acute lymphoblastic leukemia	Hematologic	6
Chronic lymphocytic leukemia	Hematologic	7
Parkinson disease	Neurodegenerative	8
Acute myeloid leukemia	Hematologic	9
Alzheimer disease	Neurodegenerative	10

Overlap of AML disease network with CDK11 inhibitor AP3 profile

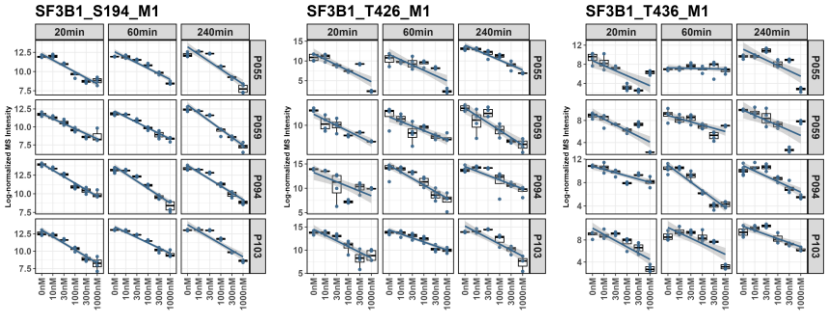


Nodes
- Disease only
- Drug only
- Overlap

Edges
- Non-overlap
- Overlap edges



Dose-dependent regulation of SF3B1 phosphorylation sites (AP3 experiments, n=4)



CDK11 INHIBITION MAY PROVIDE BROAD AML OPPORTUNITY

Beyond mutation-defined therapies in a fragmented, high-need disease

AML is broad and fragmented

~22.7k
new US cases/year

~11.5k
US deaths/year

No single mutation-defined therapy covers the disease:

FLT3	~30-40%
NPM1	~30-35%
IDH1/2	~20-25%
Spliceosome mutations	~45%

Current therapies leave open space

Venetoclax/HMA: broad backbone; resistance and myelosuppression limit durability.

FLT3 / menin: selected genotypes; resistance and durability remain open.

Gap: genotype-broad agents that combine with AML backbones

CDK11i fits a convergence point

Targets shared transcription / splicing stress biology

- Potential single agent activity across AML genotypes
- Combination rationale with venetoclax/HMA and targeted agents

T-CELL LYMPHOMAS: HIGH UNMET NEED AND CDK11 OPPORTUNITY

Peripheral T-cell lymphoma	Cutaneous T-cell lymphoma	T-ALL
~75K WW / ~11K US incidence ~40K US prevalence	~20K WW / ~3K US incidence ~16K US prevalence	~13K WW / ~2K US incidence ~20K US prevalence

DISEASE LANDSCAPE & UNMET NEED

Limited targeted innovation
- Few durable targeted treatment options in T-cell malignancies

1st line standard of care
- Chemotherapy-based; CHOP or CHP + brentuximab vedotin in CD30+ disease

Outcomes remain poor
- 5-year survival often <30% in PTCL

2nd line options limited
- Approved HDAC inhibitors / pralatexate deliver modest activity and short durability

Development opportunity
- ➢ Limited efficacy of current regimens, especially beyond 1st line

WHY CDK11 IS COMPELLING

CDK11 inhibition → **transcription + splicing stress** → **MCL1 loss and cell death**

Central role of MCL1
- PTCL frequently shows high MCL1 expression and survival dependence

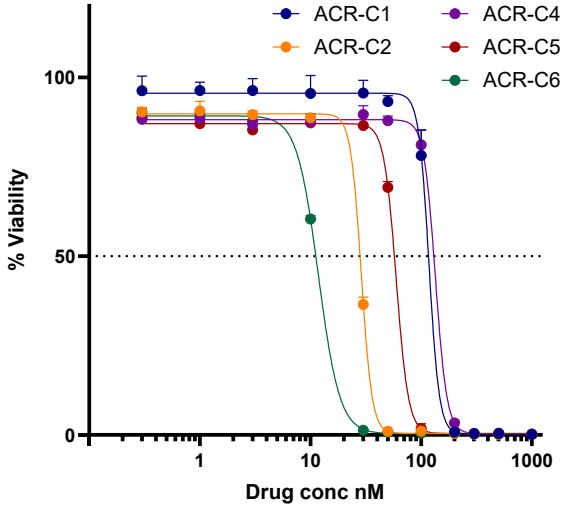
Transcriptional drivers
- STAT3/STAT5, JAK-STAT and NF-κB signaling can sustain MCL1 transcription

Potential advantage
- Suppression of MCL1 through CDK11 inhibition may offer an alternative to direct MCL1 inhibitors, which can be limited by cardiotoxicity

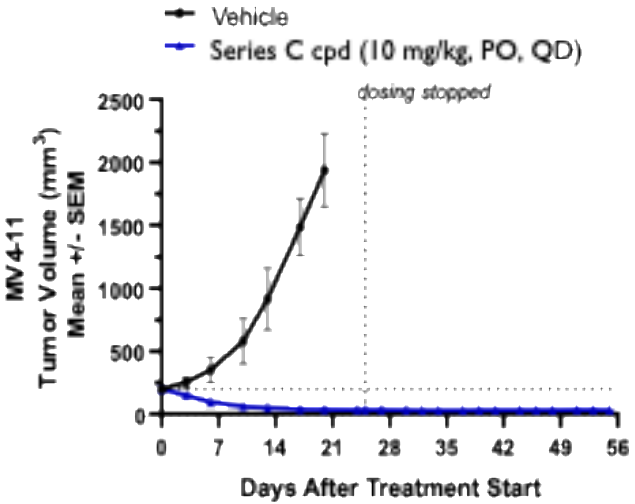
Potential positioning
- ➢ Broad opportunity across PTCL and other T-cell malignancies
- ➢ Potential combination and relapse-setting strategy

CDK11 INHIBITOR LEAD SERIES SHOWS COMPLETE AML TUMOR REGRESSION AND FAVORABLE TOLERABILITY

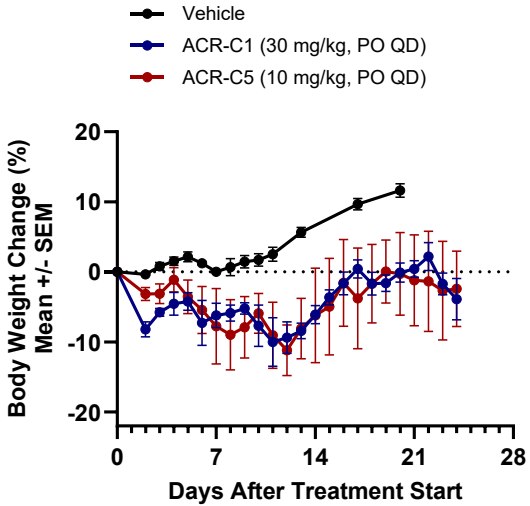
Multiple Lead Compounds



Complete Regression In Vivo



Favorable Safety Profile



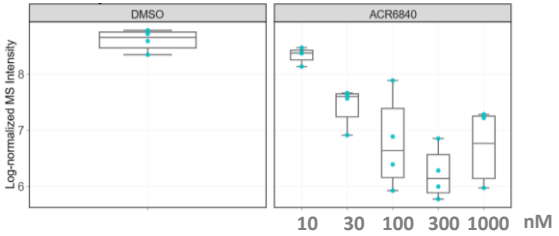
Complete tumor regression maintained after stop of dosing

CDK11 INHIBITOR ACTIVITY ALONE AND IN COMBINATION WITH BCL-2 FAMILY INHIBITORS IN HEMATOLOGICAL MALIGNANCIES

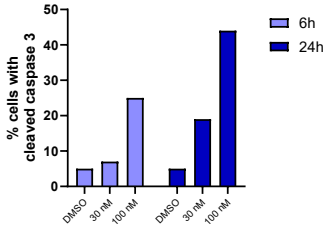
Rationale: CDK11 inhibition sensitizes tumors to BCL-2 family inhibitors through MCL1 downregulation and dysregulated splicing

- Dysregulated splicing of anti-apoptotic transcripts to pro-apoptotic (Bcl-xL to Bcl-xS) providing strong rationale for combination with BCL2 inhibitors

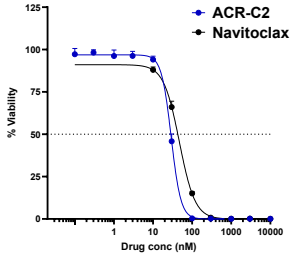
ACR CDK11 inhibitors reduce levels of anti-apoptotic MCL1 (AP3 global proteomics analysis)

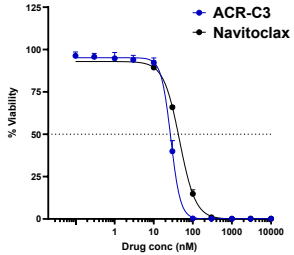


CDK11 inhibitors induce apoptosis in aggressive AML cell line MV4-11

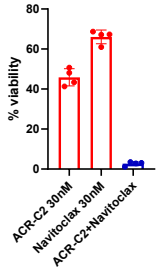


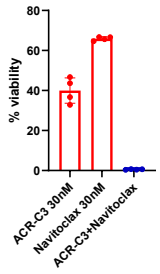
ACR CDK11 inhibitors are as potent as BCL-2 inhibitor in AML model





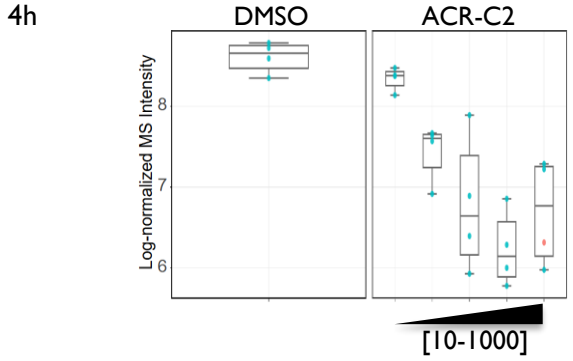
ACR CDK11 inhibitors exhibit synergistic activity with BCL-2 inhibitors in AML model

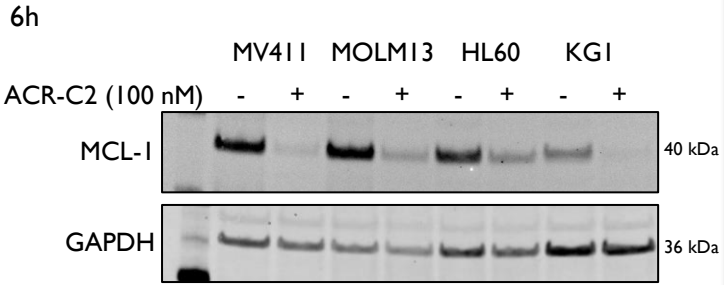




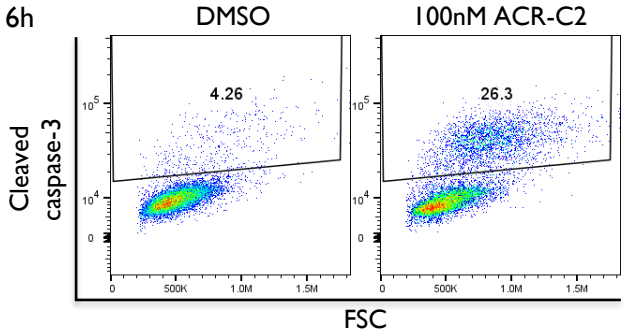
ACR-C2 DOWNREGULATES ANTI-APOPTOTIC MCL-1 PROTEIN AND INDUCES CELL DEATH AFTER 6H TREATMENT

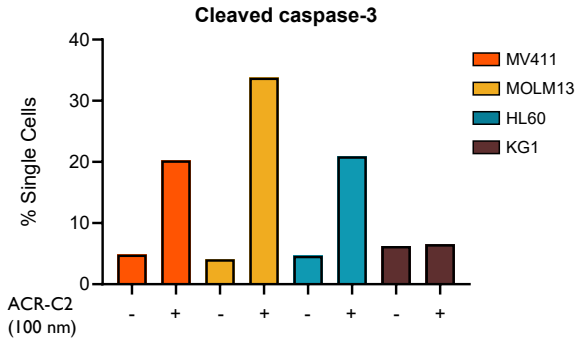
Pan MCL-1 levels



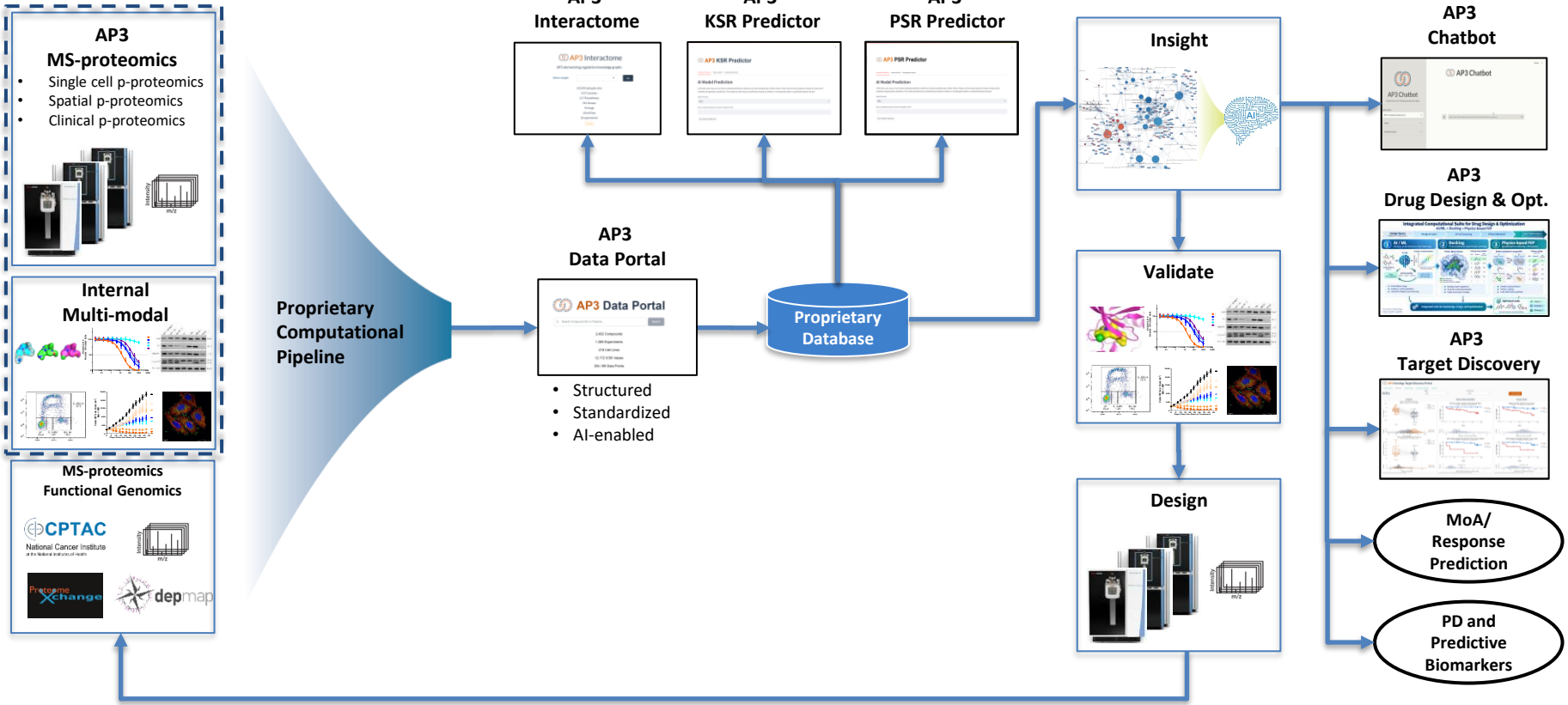


% Cleaved caspase-3 positive cells at 6h - flow cytometry





AP3 GENERATIVE PHOSPHOPROTEOMICS PLATFORM



AP3 INTERACTOME: PROPRIETARY INTERACTIVE DATA ANALYSIS INFRASTRUCTURE FOR ALL ACRIVON DATA AND EXPERIMENTS

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

~164,000 phosphosites

Data completeness Peptide IDs CV

Pearson Correlation

PCA Hierarchical Clustering

~50,000 phosphosites

Filtering Batch effects Normalization Imputation

ANOVA Hierarchical clustering

DEPs Volcano Plots

Consensus Sequence Motif

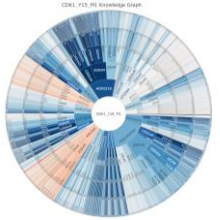
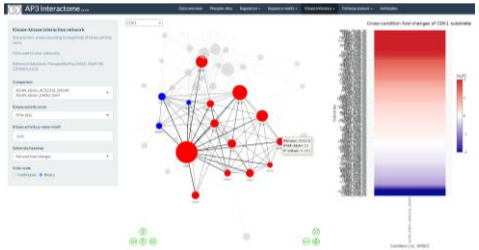
Pathway Enrichment

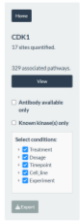
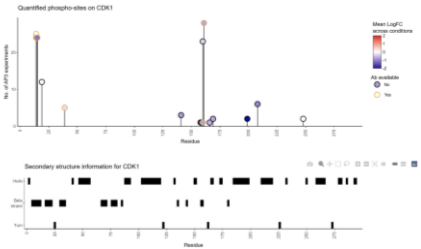
Kinase Inference

Network Mapping

Biomarkers Machine-Learning



DATA DRIVEN EXECUTION AND VALUE CREATION

Recent Accomplishments (Last 12 Months)

- ✓ Continued positive ACR-368 data in ongoing registrational intent EC trial (April 2025 and January 2026 Corporate R&D Events)
- ✓ Strong enthusiasm for promising ACR-368 clinical data at 2026 ESGO late breaking oral presentation and corporate live KOL expert panel (Q1 2026)
- ✓ cORR of 52% observed in serous EC, a high unmet need disease w/ limited treatment options contributing to ~50% of all EC mortality
- ✓ Ongoing prospective enrollment (US + EU) in serous EC (biopsy independent) Arm 3 (ACR-368 + ULDG) in Phase 2b trial (Q4 2025)
- ✓ Ongoing prospective enrollment (US + EU) in serous EC (biopsy independent) Arm 4 (ACR-368) in Phase 2b trial (Q2 2026)
- ✓ 4 presentations showcasing expanded AP3 capabilities and compelling ACR-2316 preclinical data (AACR Q2 2025 and AACR-NCI-EORTC Q4 2025)
- ✓ Provided ACR-2316 Phase 1/2 dose escalation clinical data and transitioned into randomized dose expansion in AP3-identified solid tumor types (Q3 2026)

Anticipated Next Milestones

ACR-368 (Phase 2b)

- Prespecified simultaneous interim analysis and data update from both all-comer (biopsy-independent) serous EC arms of the ACR-368 Phase 2b study in second half of 2026
- Initiate Phase 3 confirmatory trial for ACR-368 in first half of 2027
- Based on interim data read-out, complete enrollment of the registrational intent all-comer (biopsy-independent) serous EC Arm 3 or Arm 4 by fourth quarter of 2026

ACR-2316 (Phase 1/2)

- ✓ Additional ACR-2316 Phase 1/2 clinical data for weekly and bi-weekly dosing regimens and transition into dose expansion in AP3-identified tumor types in 2026

Earlier Pipeline

- Submit IND filing to the FDA for CDK11 inhibitor development candidate in first half of 2027
- Initiate additional internal programs utilizing the AP3 platform in 2026

FINANCIAL HIGHLIGHTS

Cash and Investments

$90.0M

Balance sheet 30-Jun-2026

Projected runway into

Q4 2027

Current operating plan, assuming no additional financing

Fully Diluted Shares Outstanding

52.0M

Shares and equity grants outstanding 30-Jun-2026

Note: unaudited