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.

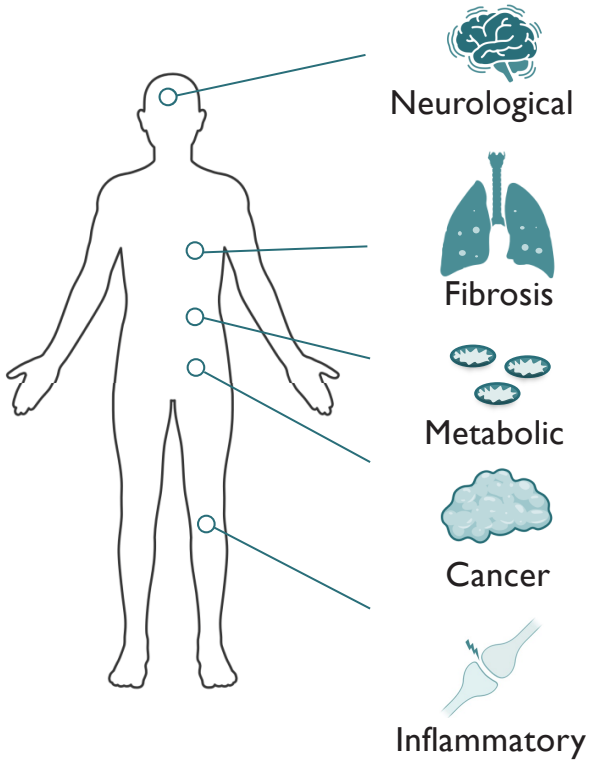
You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this presentation. We undertake no obligation to update any forward-looking statements or to reflect new information or the occurrence of unanticipated events, except as required by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

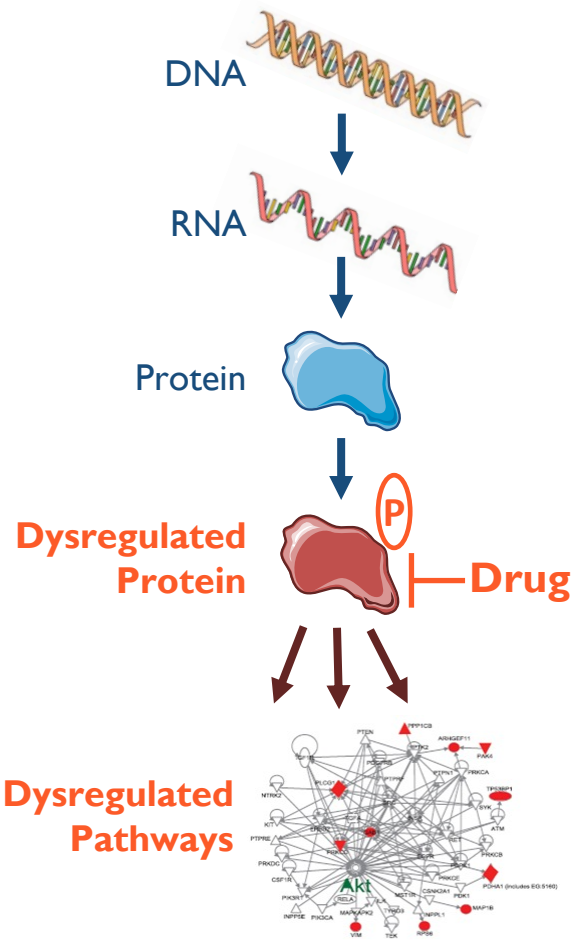
OUTLINE

- 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

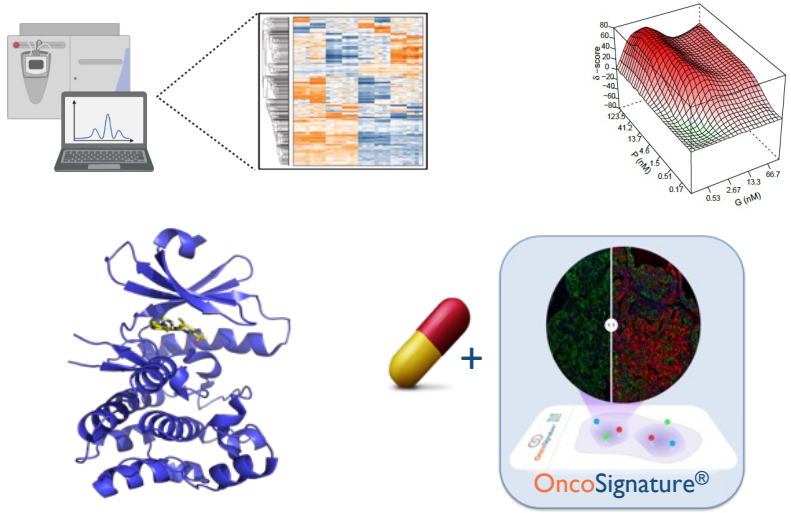
ACRIVON THERAPEUTICS – A NEXT-GENERATION PRECISION MEDICINE COMPANY





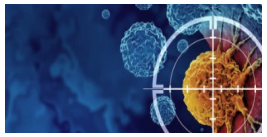
Acrivon Predictive Precision Proteomics (AP3)

- 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



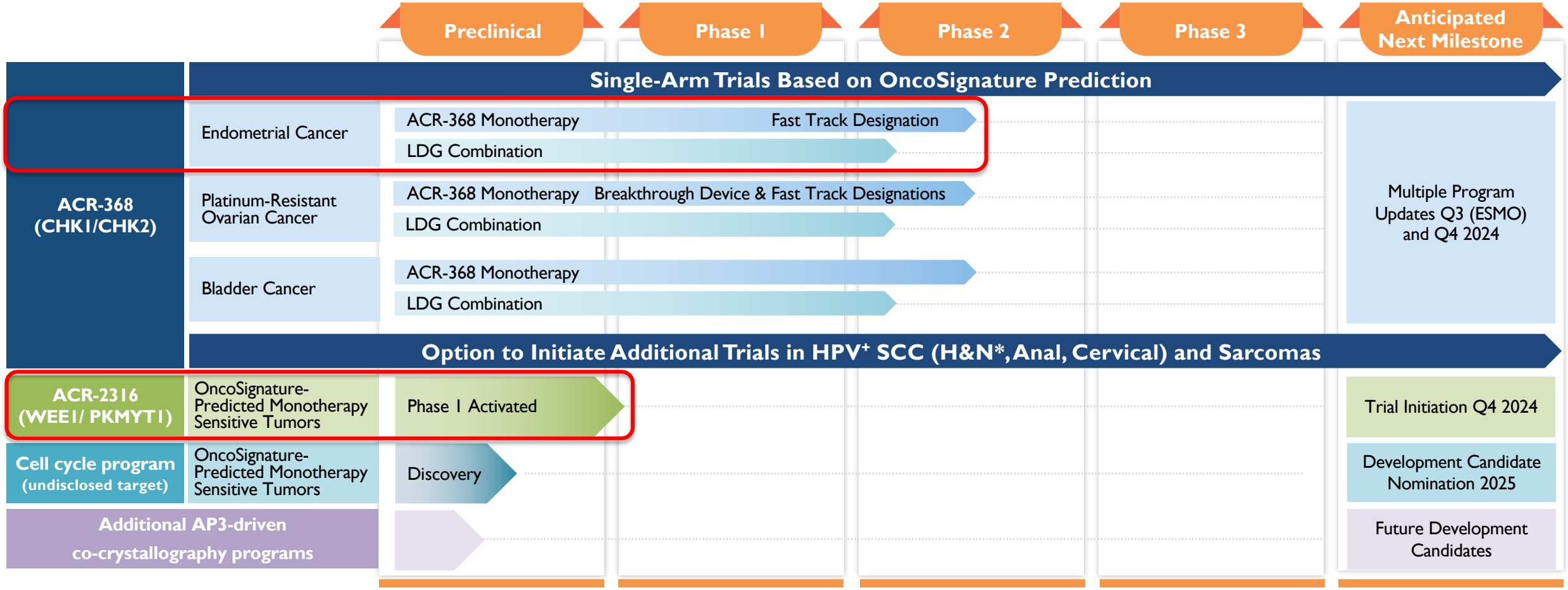
Blume-Jensen, P &Hunter, T: Oncogenic kinase signaling *Nature* (2001)
Olsen, JV et al: Global, in vivo, and site-specific phosphorylation dynamics in signaling networks *Cell* (2006);
Andersen, JN et al: Pathway-based identification of biomarkers for targeted therapeutics: personalized oncology with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

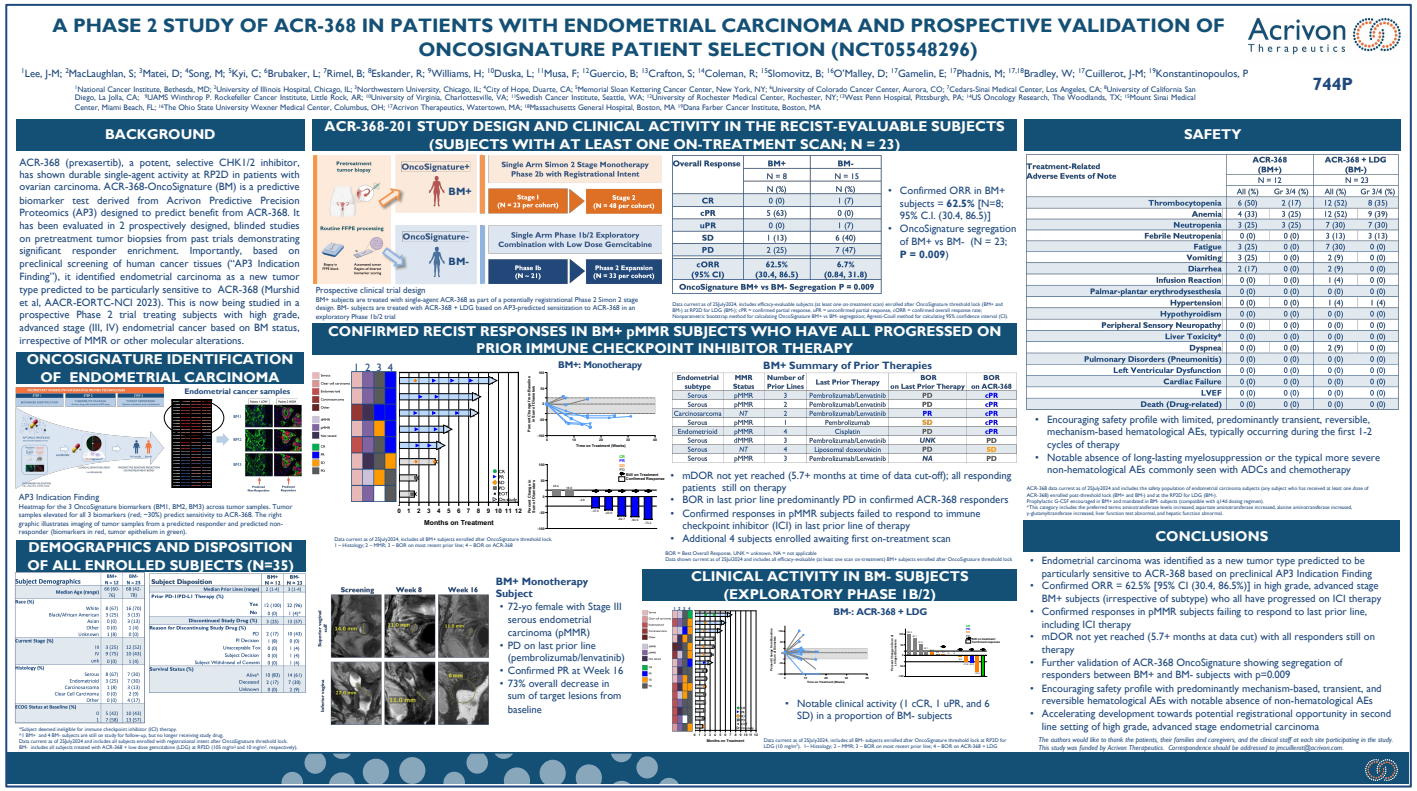
ACRIVON PIPELINE



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



A PHASE 2 STUDY OF ACR-368 IN PATIENTS WITH ENDOMETRIAL CARCINOMA AND PROSPECTIVE VALIDATION OF ONCOSIGNATURE PATIENT SELECTION (NCT05548296)

Acrivon Therapeutics

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[1]Lee, J-M; [2]MacLaughlan, S; [3]Matei, D; [4]Song, M; [5]Kyi, C; [6]Brubaker, L; [7]Rimel, B; [8]Eskander, R; [9]Williams, H; [10]Duska, L; [11]Musa, F; [12]Guercio, B; [13]Crafton, S; [14]Coleman, R; [15]Slomovitz, B; [16]O'Malley, D; [17]Gamelin, E; [17]Phadnis, M; [17,18]Bradley, W; [17]Cuillerot, J-M; [19]Konstantinopoulos, P

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BACKGROUND

ACR-368 (prexasertib), a potent, selective CHK1/2 inhibitor, has shown durable single-agent activity at RP2D in patients with ovarian carcinoma. ACR-368-OncoSignature (BM) is a predictive biomarker test derived from Acrivon Predictive Precision Proteomics (AP3) designed to predict benefit from ACR-368. It has been evaluated in 2 prospectively designed, blinded studies on pretreatment tumor biopsies from past trials demonstrating significant responder enrichment. Importantly, based on preclinical screening of human cancer tissues ("AP3 Indication Finding"), it identified endometrial carcinoma as a new tumor type predicted to be particularly sensitive to ACR-368 (Murshid et al, AACR-EORTC-NCI 2023). This is now being studied in a prospective Phase 2 trial treating subjects with high grade, advanced stage (III, IV) endometrial cancer based on BM status, irrespective of MMR or other molecular alterations.

ONCOSIGNATURE IDENTIFICATION OF ENDOMETRIAL CARCINOMA

AP3 Indication Finding

Heatmap for the 3 OncoSignature biomarkers (BM1, BM2, BM3) across tumor samples. Tumor samples elevated for all 3 biomarkers (red; ~30%) predict sensitivity to ACR-368. The right graphic illustrates imaging of tumor samples from a predicted responder and predicted non-responder (biomarkers in red, tumor epithelium in green).

DEMOGRAPHICS AND DISPOSITION OF ALL ENROLLED SUBJECTS (N=35)

Subject Demographics	BM+ N = 12	BM- N = 23
Median Age (range)	66 (40-76)	68 (42-78)
Race (%)		
White	8 (67)	16 (70)
Black/African American	3 (25)	5 (22)
Asian	0 (0)	0 (0)
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 immune checkpoint inhibitor (ICI) 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 after OncoSignature threshold lock. BM- includes all subjects treated with ACR-368 + low dose gemcitabine (LDG) at RP2D (100 mg/m² and 50 mg/m², respectively).

ACR-368-201 STUDY DESIGN AND CLINICAL ACTIVITY IN THE RECIST-EVALUABLE SUBJECTS (SUBJECTS WITH AT LEAST ONE ON-TREATMENT SCAN; N = 23)

Prospective clinical trial design

BM+ subjects are treated with single-agent ACR-368 as part of a potentially registrational Phase 2 Simon 2 stage design. BM- subjects are treated with ACR-368 + LDG based on AP3-predicted sensitization to ACR-368 in an exploratory Phase 1b/2 trial

Overall Response	BM+ N = 8 N (%)	BM- N = 15 N (%)
CR	0 (0)	1 (7)
cPR	5 (63)	0 (0)
uPR	0 (0)	1 (7)
SD	1 (13)	6 (40)
PD	2 (25)	7 (47)
cORR (95% CI)	62.5% (30.4, 86.5)	6.7% (0.84, 31.8)

OncoSignature BM+ vs BM- Segregation P = 0.009

- Confirmed ORR in BM+ subjects = **62.5%** [N=8; 95% C.I. (30.4, 86.5)]
- OncoSignature segregation of BM+ vs BM- (N = 23; **P = 0.009**)

Data current as of 25July2024, includes efficacy-evaluable subjects (at least one on-treatment scan) enrolled after OncoSignature threshold lock (BM+ and BM-) at RP2D for LDG (BM-); cPR = confirmed partial response, uPR = unconfirmed partial response, cORR = confirmed overall response rate; Nonparametric bootstrap method for calculating OncoSignature BM+ vs BM- segregation; Agresti-Coull method for calculating 95% confidence interval (CI).

CONFIRMED RECIST RESPONSES IN BM+ pMMR SUBJECTS WHO HAVE ALL PROGRESSED ON PRIOR IMMUNE CHECKPOINT INHIBITOR THERAPY

BM+: Monotherapy

BM+ Summary of Prior Therapies

Endometrial subtype	MMR Status	Number of Prior Lines	Last Prior Therapy	BOR on Last Prior Therapy	BOR on ACR-368
Serous	pMMR	3	Pembrolizumab/Lenvatinib	PD	cPR
Serous	pMMR	2	Pembrolizumab/Lenvatinib	PD	cPR
Carcinosarcoma	NT	2	Pembrolizumab/Lenvatinib	PR	cPR
Serous	pMMR	1	Pembrolizumab	SD	cPR
Endometrioid	pMMR	4	Cisplatin	PD	cPR
Serous	dMMR	3	Pembrolizumab/Lenvatinib	UNK	PD
Serous	NT	4	Liposomal doxorubicin	PD	SD
Serous	pMMR	3	Pembrolizumab/Lenvatinib	NA	PD

- mDOR not yet reached (5.7+ months at time of data cut-off); all responding patients still on therapy
- BOR in last prior line predominantly PD in confirmed ACR-368 responders
- Confirmed responses in pMMR subjects failed to respond to immune checkpoint inhibitor (ICI) in last prior line of therapy
- Additional 4 subjects enrolled awaiting first on-treatment scan

BOR = Best Overall Response, UNK = unknown, NA = not applicable
Data shown current as of 25July2024 and includes all efficacy-evaluable (at least one scan on-treatment) BM+ subjects enrolled after OncoSignature threshold lock

BM+ Monotherapy Subject

- 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

CLINICAL ACTIVITY IN BM- SUBJECTS (EXPLORATORY PHASE 1B/2)

BM-: ACR-368 + LDG

- Notable clinical activity (1 cCR, 1 uPR, and 6 SD) in a proportion of BM- subjects

Data current as of 25July2024, includes all BM- subjects enrolled after OncoSignature threshold lock at RP2D for LDG (6 mg/m²). 1= Histology; 2 – MMR; 3 – BOR on most recent prior line; 4 – BOR on ACR-368 + LDG

SAFETY

Treatment-Related Adverse Events of Note	ACR-368 (BM+) N = 12 All (%)	ACR-368 (BM+) N = 12 Gr 3/4 (%)	ACR-368 + LDG (BM-) N = 23 All (%)	ACR-368 + LDG (BM-) N = 23 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)	0 (0)	3 (13)	3 (13)
Fatigue	3 (25)	0 (0)	7 (30)	0 (0)
Vomiting	3 (25)	0 (0)	2 (9)	0 (0)
Diarrhea	2 (17)	0 (0)	2 (9)	0 (0)
Infusion Reaction	0 (0)	0 (0)	1 (4)	0 (0)
Palmar-plantar erythrodysesthesia	0 (0)	0 (0)	0 (0)	0 (0)
Hypertension	0 (0)	0 (0)	1 (4)	1 (4)
Hypothyroidism	0 (0)	0 (0)	0 (0)	0 (0)
Peripheral Sensory Neuropathy	0 (0)	0 (0)	0 (0)	0 (0)
Liver Toxicity*	0 (0)	0 (0)	0 (0)	0 (0)
Dyspnea	0 (0)	0 (0)	2 (9)	0 (0)
Pulmonary Disorders (Pneumonitis)	0 (0)	0 (0)	0 (0)	0 (0)
Left Ventricular Dysfunction	0 (0)	0 (0)	0 (0)	0 (0)
Cardiac Failure	0 (0)	0 (0)	0 (0)	0 (0)
LVEF	0 (0)	0 (0)	0 (0)	0 (0)
Death (Drug-related)	0 (0)	0 (0)	0 (0)	0 (0)

- Encouraging safety profile with limited, predominantly transient, reversible, mechanism-based hematological AEs, typically occurring 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

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 post-threshold lock (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).
*This category includes the preferred terms aminotransferase levels increased, aspartate aminotransferase increased, alanine aminotransferase increased, γ-glutamyltransferase increased, liver function test abnormal, and hepatic function abnormal.

CONCLUSIONS

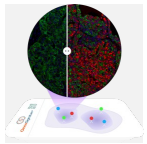
- Endometrial carcinoma was identified as a new tumor type predicted to be particularly sensitive to ACR-368 based on preclinical AP3 Indication Finding
- Confirmed ORR = 62.5% (95% CI (30.4, 86.5%)) in high grade, advanced stage BM+ subjects (irrespective of subtype) who all have progressed on ICI therapy
- Confirmed responses in pMMR subjects failing to respond to last prior line, including ICI therapy
- mDOR not yet reached (5.7+ months at data cut) with all responders still on therapy
- Further validation of ACR-368 OncoSignature showing segregation of responders between BM+ and BM- subjects with p=0.009
- Encouraging safety profile with predominantly mechanism-based, transient, and reversible hematological AEs with notable absence of non-hematological AEs
- Accelerating development towards potential registrational opportunity in second line setting of high grade, advanced stage endometrial carcinoma

The authors would like to thank the patients, their families and caregivers, and the clinical staff at each site participating in the study. This study was funded by Acrivon Therapeutics. *Correspondence should be addressed to jmcallester@acrivon.com.*

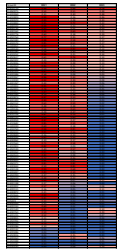
Data cut as of July 25, 2024

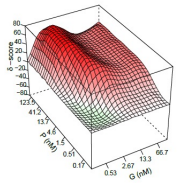
Poster available on Acrivon's website: https://acrivon.com/science/#publications-posters

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



OncoSignature®





Clinical Biomarkers
Predictive OncoSignature tests

Indication Finding
Sensitive tumor types

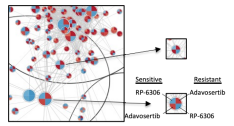
Resistance Mechanisms
Rational drug combinations

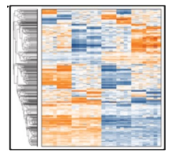
AP3

Drug Discovery SAR
Optimal target selectivity

PD Markers
~6,000 per compound

Informs in-licensing
AP3 profiling of candidates





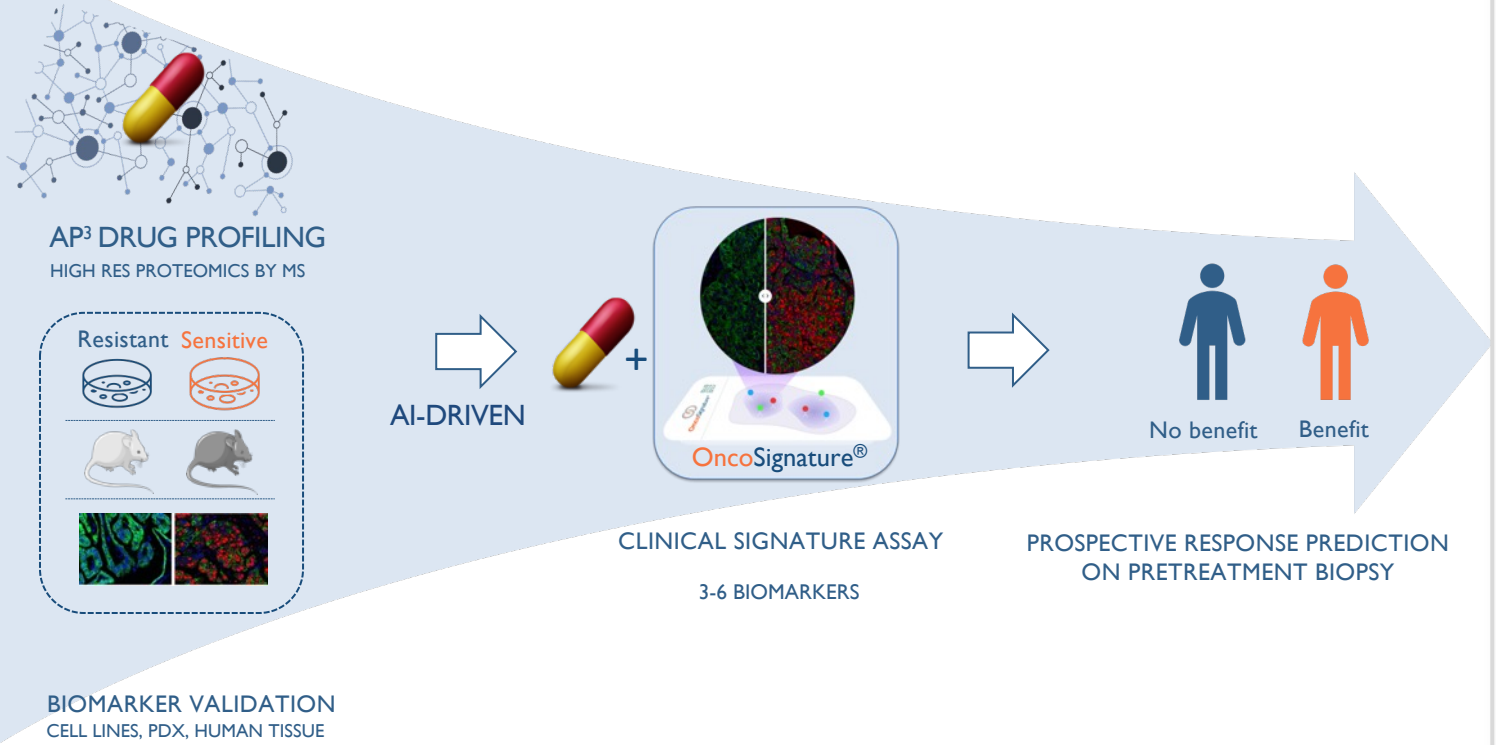
Streamlined Clinical Development
Predicted sensitive indications with informed dose optimization

Predicted Responder

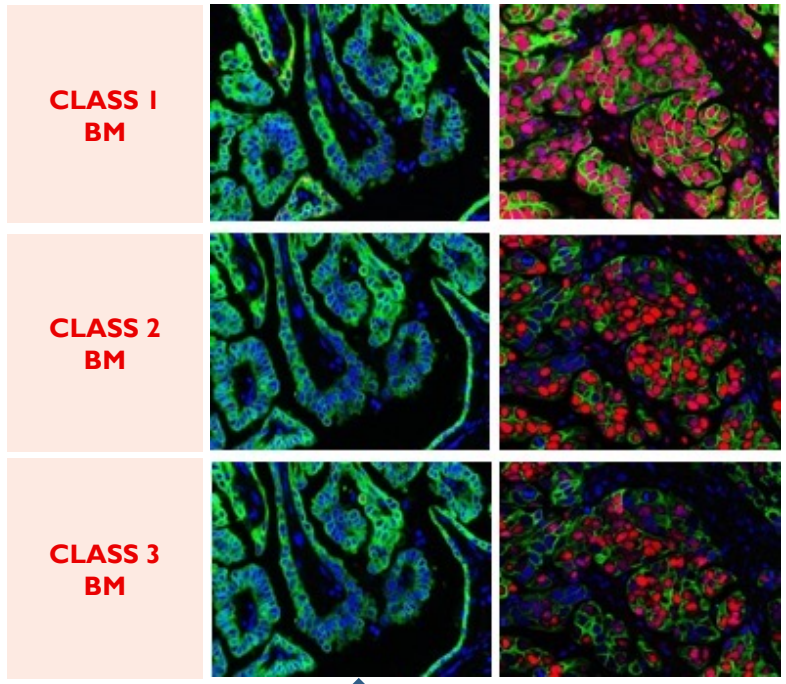
AP3 PLATFORM: DRUG RESPONSE PREDICTION IN INDIVIDUAL PATIENTS

PROPRIETARY WORKFLOW INTEGRATING PROVEN TECHNOLOGIES

STEP 1	STEP 2	STEP 3
BIOMARKER IDENTIFICATION	THERAPEUTIC PACKAGE Acrivon drug with predictive BM assay	PATIENT RESPONDERS Optimal indications and combinations



OncoSignature®

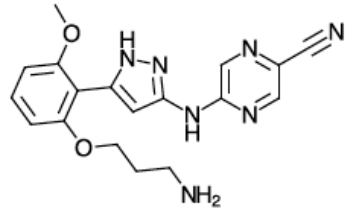


Patients without biomarkers critical for drug sensitivity efficiently excluded

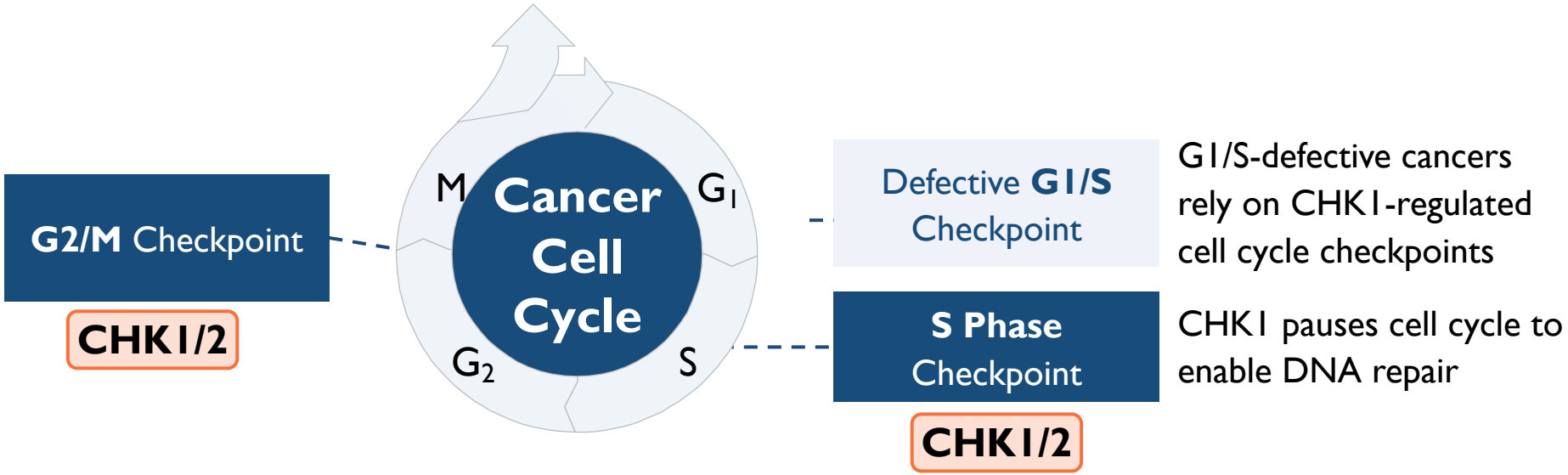
"Disease Pathway-Based Method to Generate Biomarker Panels Tailored to Specific Therapeutics for Individualized Treatments": EP 2 229 589, issued June 10, 2015; US2017/0067877A9, pending. OncoSignature® *is a Registered Trademark: US Reg. No. 5,718,472; Int. Cl. 5, 42. Intl. Reg. 1382289*

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

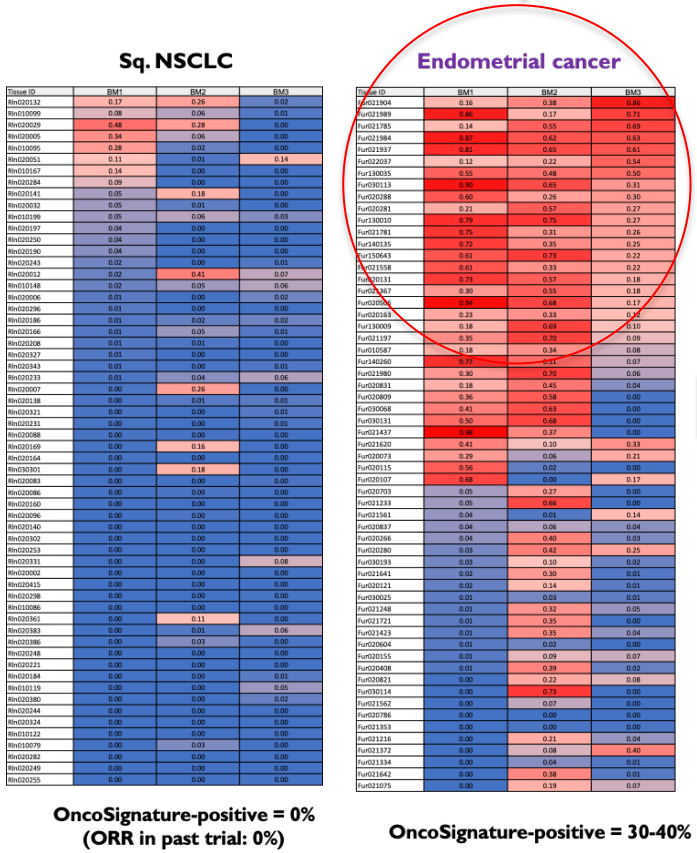
ENDOMETRIAL CANCER IS AN AP3-PREDICTED ACR-368-SENSITIVE TUMOR

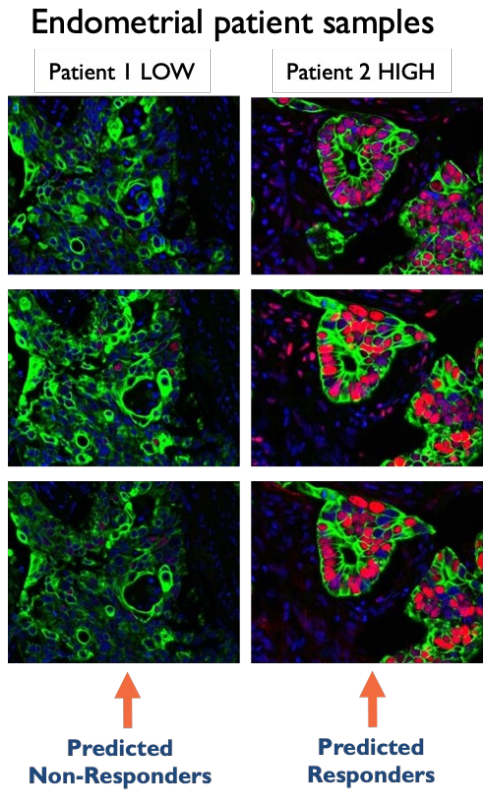
ACR-368 OncoSignature-based indication finding prior to trial entry

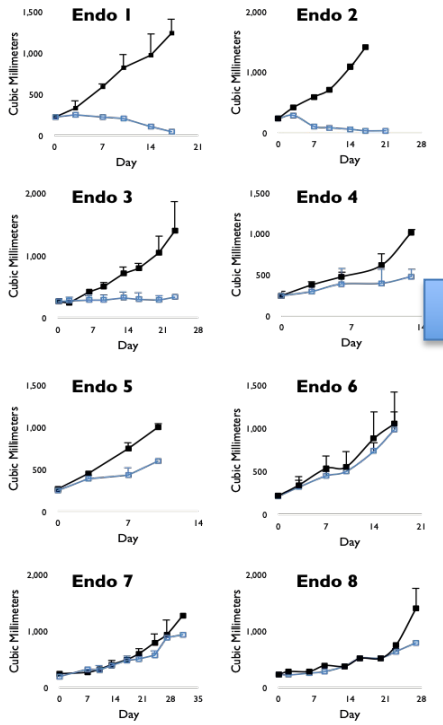
ACR-368 OncoSignature imaging demonstrates addiction to CHK1/2 DDR axis

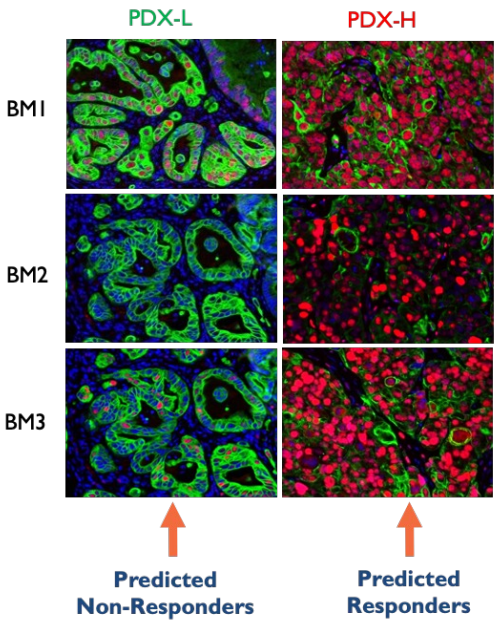
Confirmation of predicted sensitivity in genetically non-modified PDX models

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]

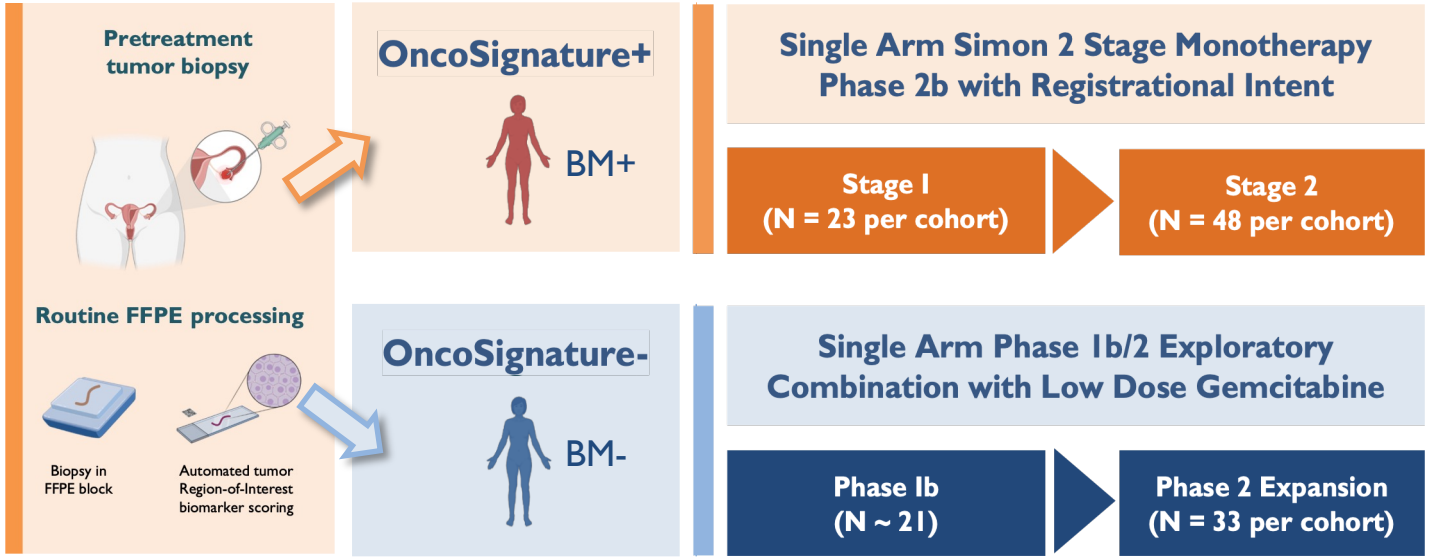
ACR-368 Target Product Profile:

- ≥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-1therapy.
^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)

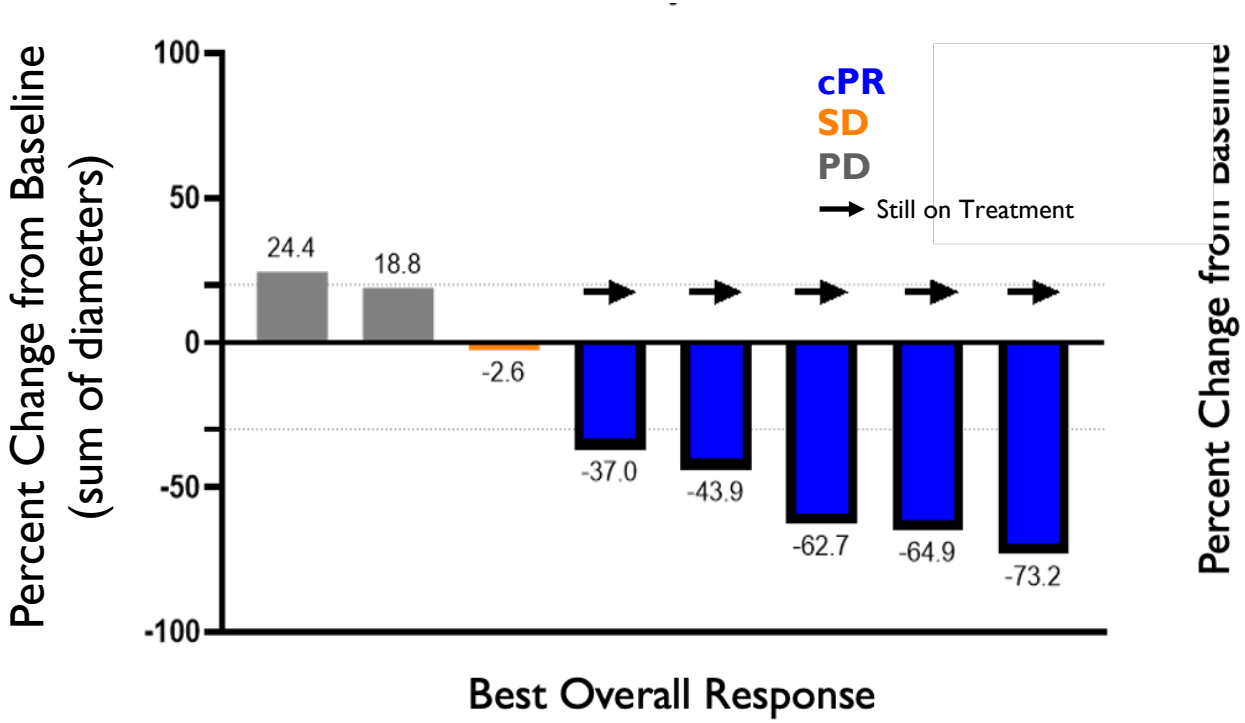
Overall Response	BM+ Monotherapy	BM- LDG Combination	Total
	N = 8	N = 15	N=23
	N (%)	N (%)	N (%)
CR	0 (0)	1 (7)	1 (4)
cPR	5 (63)	0 (0)	5 (22)
uPR	0 (0)	1 (7)	1 (4)
SD	1 (13)	6 (40)	7 (30)
PD	2 (25)	7 (47)	9 (39)
cORR (95% CI)	**62.5% (30.4, 86.5)**	**6.7% (0.84, 31.8)**	**26% (12.3,46.8)**
OncoSignature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

[1]Subjects with ≥1 on-treatment scan

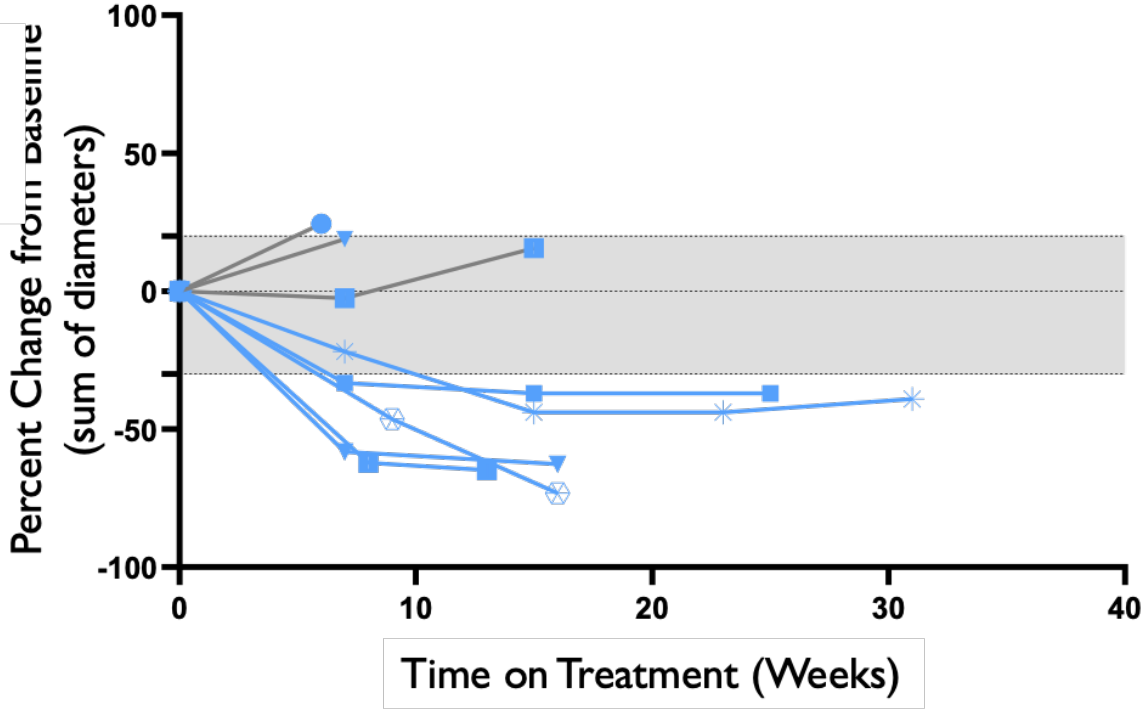
[2]https://ir.acrivon.com/news-events/events-presentations

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%)

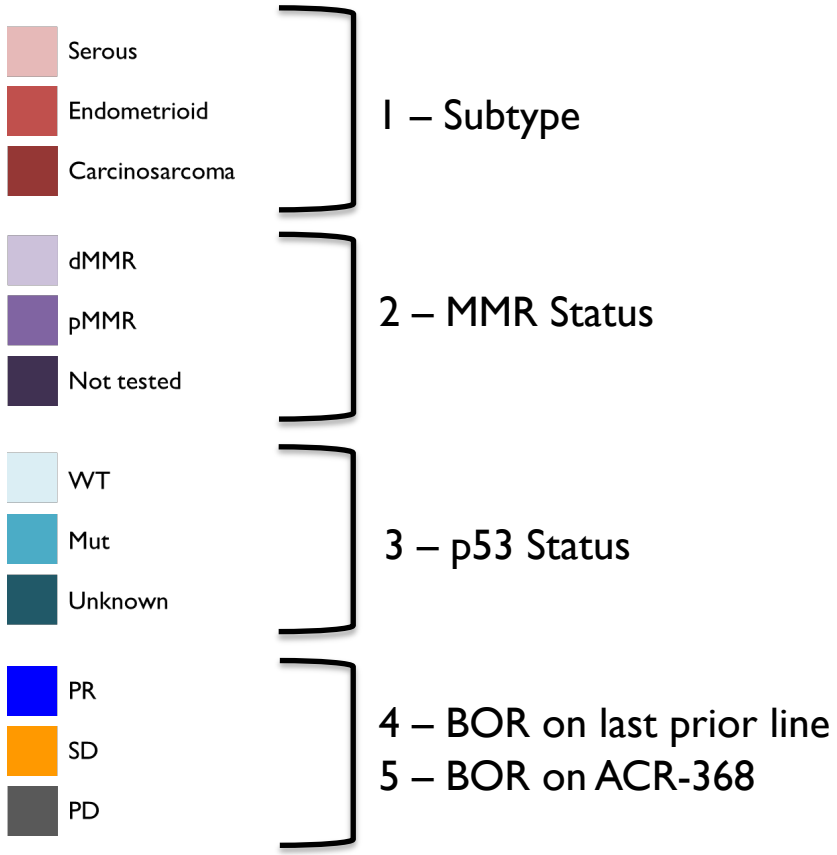


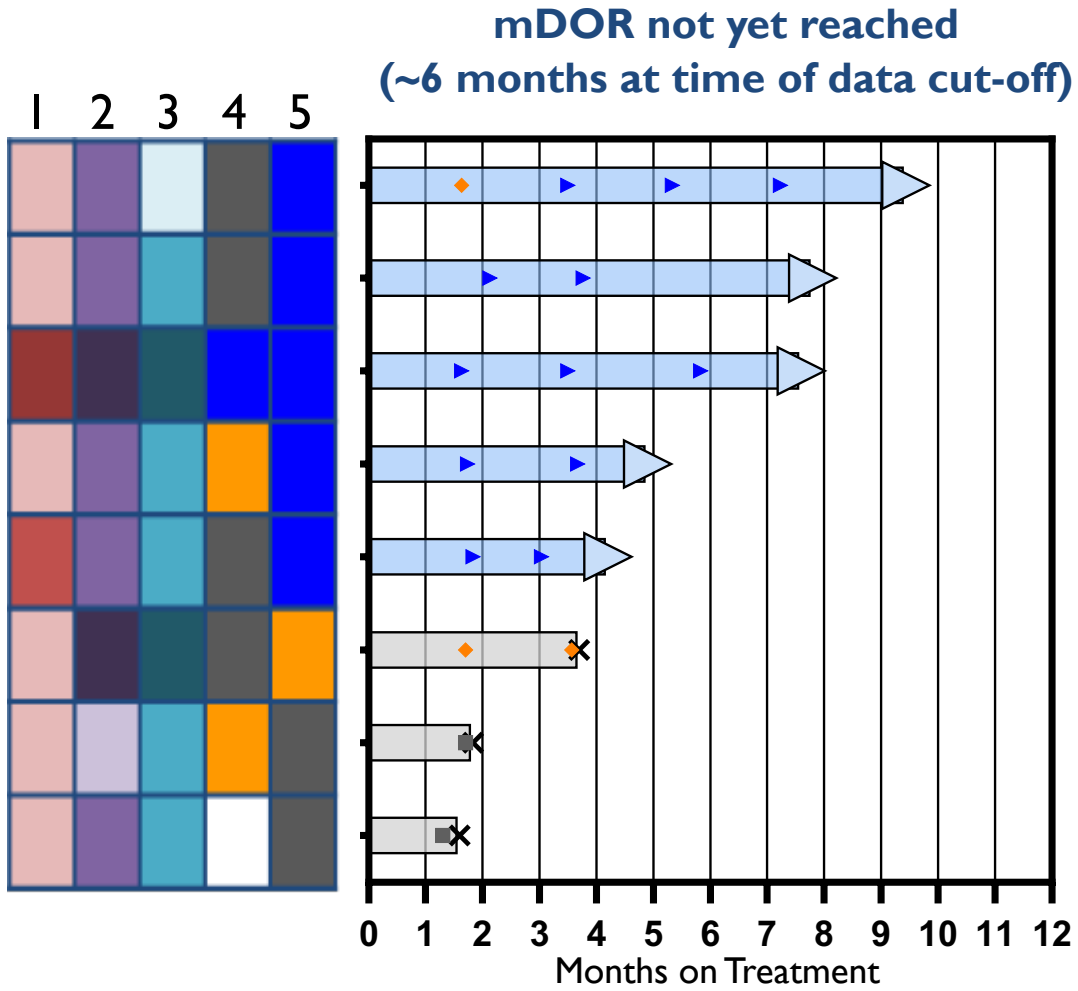
Significant disease control (75%) with most RECIST responses occurring early



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

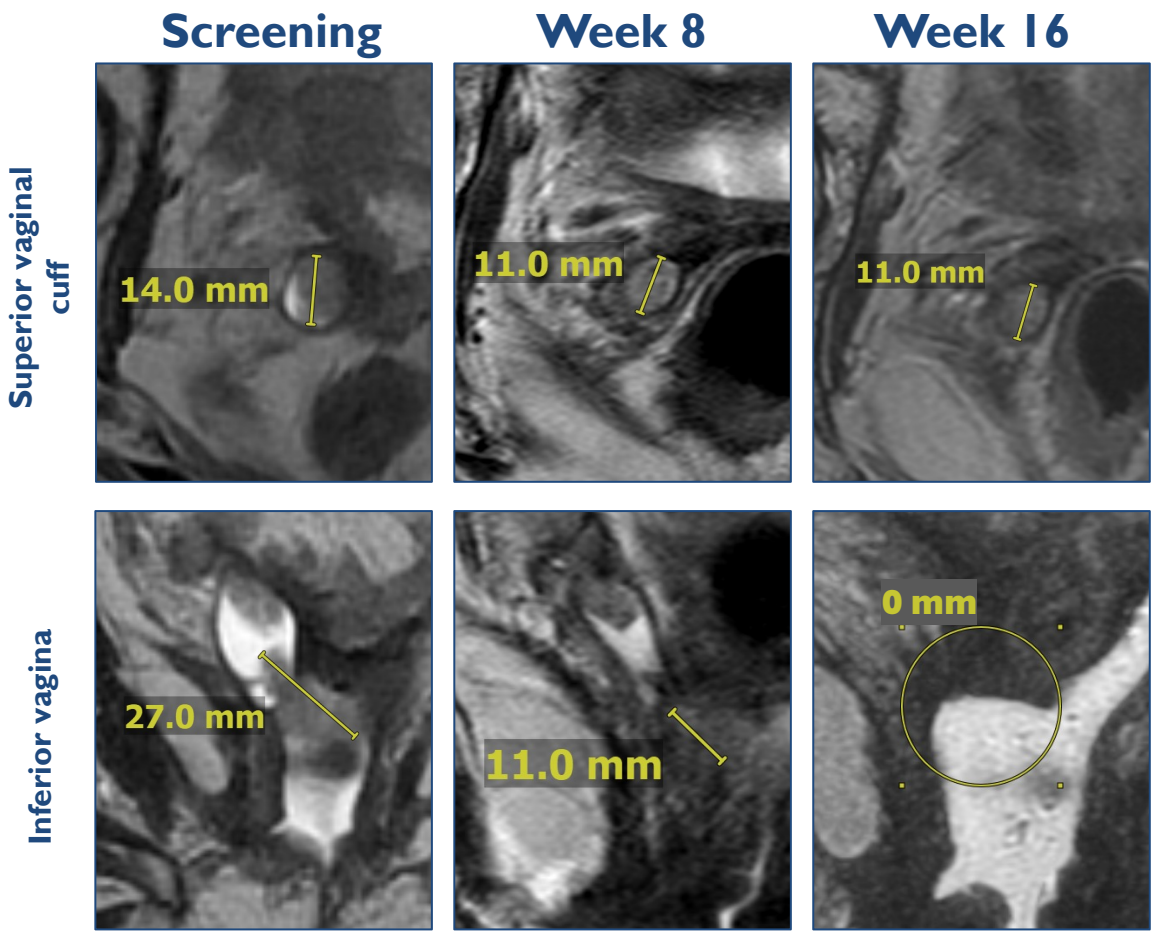
CONFIRMED RESPONSES IN SUBJECTS WHO ALL PROGRESSED ON PRIOR ANTI-PD-1

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

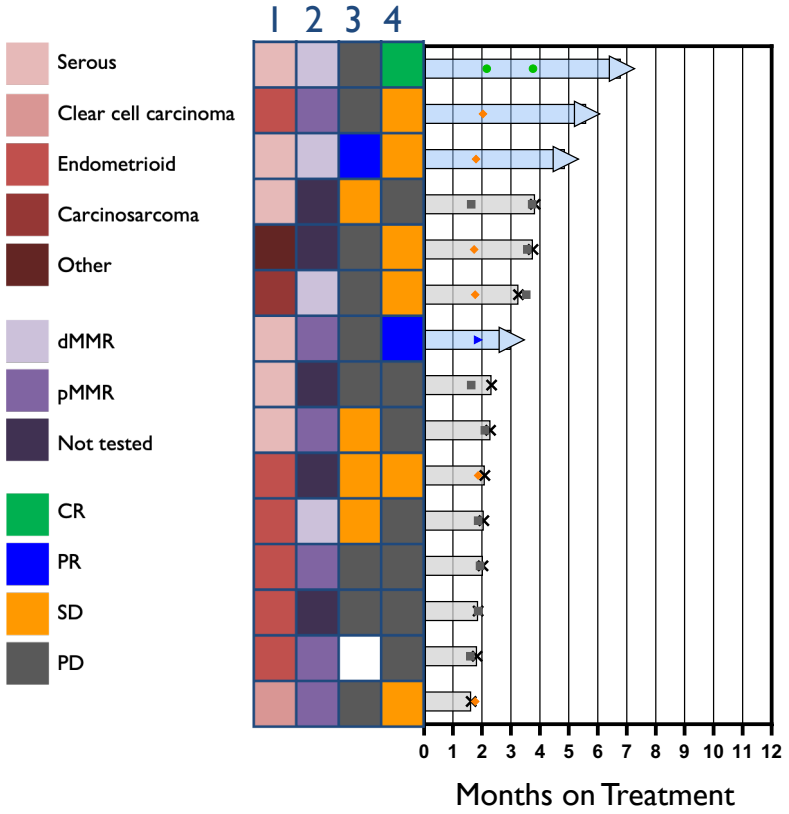
BOR = Best Overall Response, UNK = unknown, NA = not applicable, NT = not tested
Data shown current as of 25Jul2024 and includes all efficacy-evaluable (at least one scan on-treatment) BM+ subjects

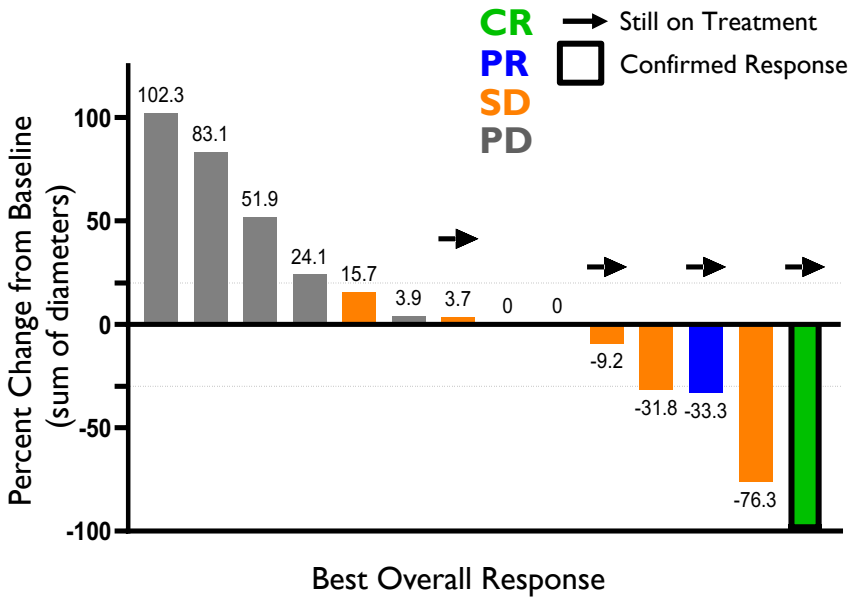
DEEP, RAPID RESPONSES SEEN IN PATIENTS WITH LARGE TUMOR LESIONS

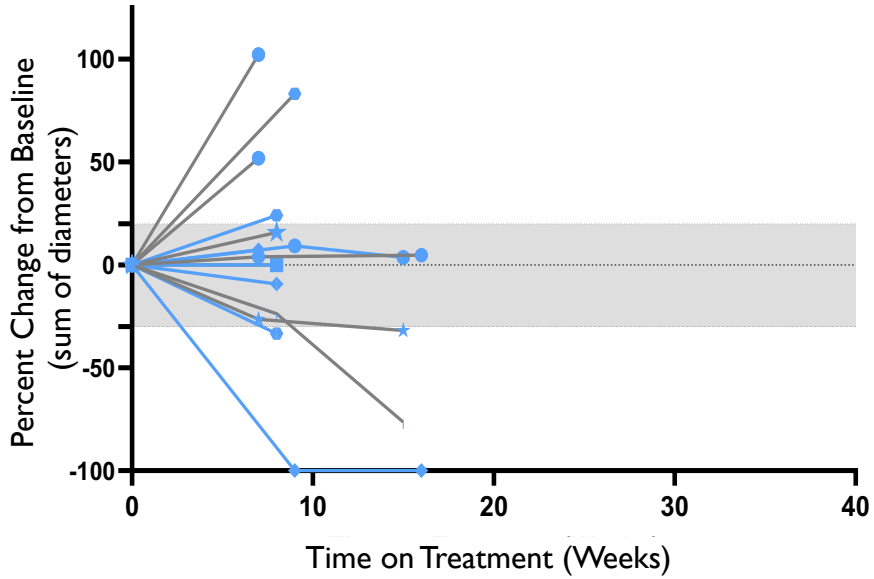


- 72-yo female with Stage III serous endometrial carcinoma (pMMR)
- PD on last prior line (pembrolizumab/lenvatinib)
- Confirmed PR at Week 16
- 73% overall decrease in sum of target lesions from baseline

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/m^2).
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+)**		**ACR-368 + LDG (BM-)**	
	N = 12		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

- <u>Second line (2L) now represents a high unmet need</u>
  - 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

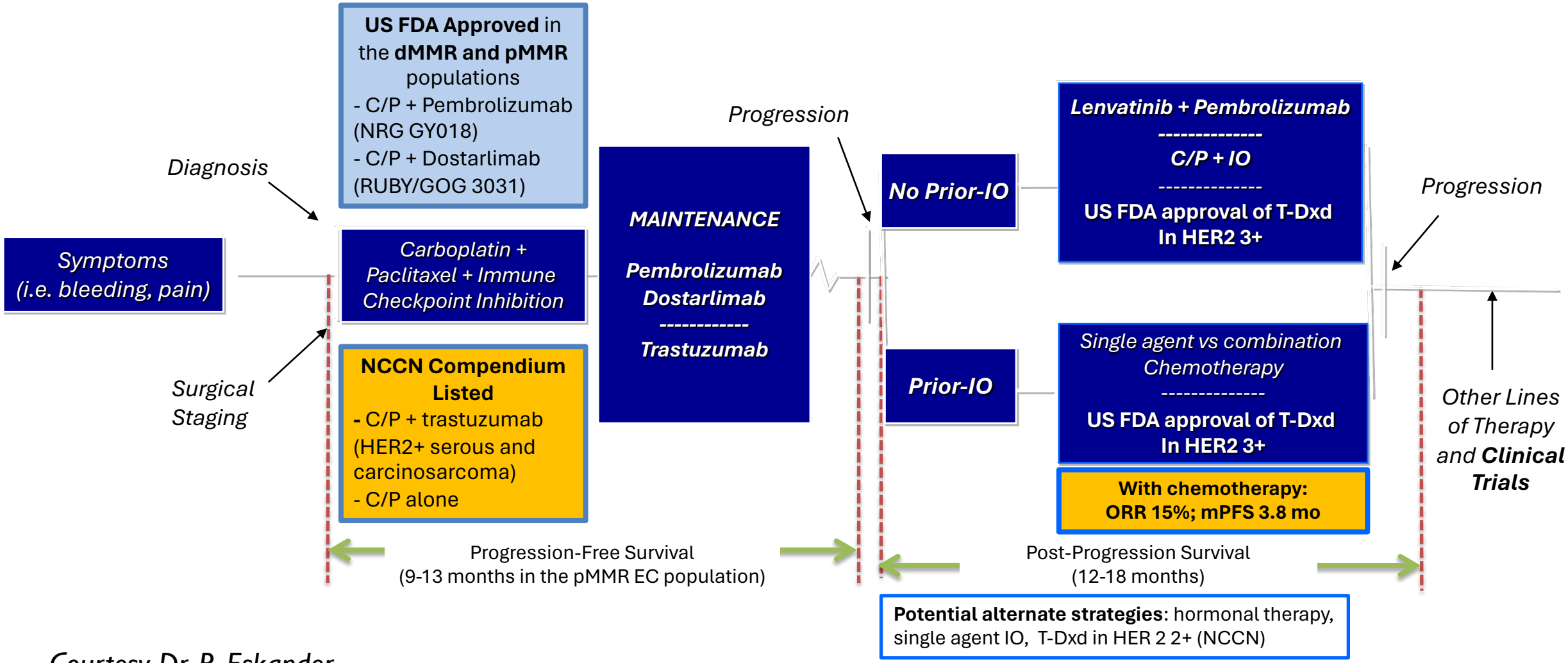
[1]Eskander et al, NEJM 2023; [2]Mirza et al, NEJM 2023; [3]Makker et al, NEJM 2022

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

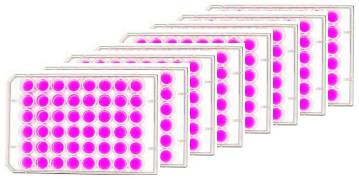
AP3-BASED DRUG DISCOVERY

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

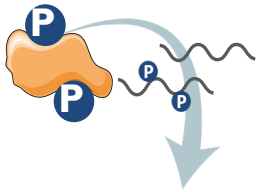
IND CLEARED AND FIRST CLINICAL SITES ACTIVATED AHEAD OF SCHEDULE

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

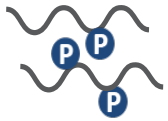
Drug treatment



Proteolysis
P-peptide enrichment

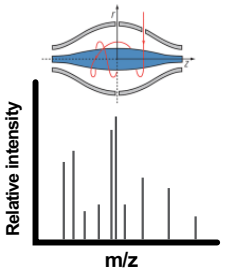


Peptide clean up



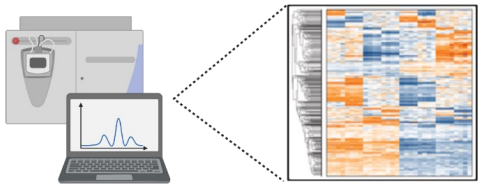
Ultra high resolution
P-proteomic profiling

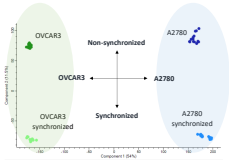
Direct DIA analysis



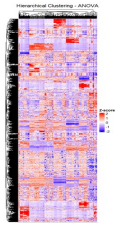
High resolution and throughput MS-based P-proteomics

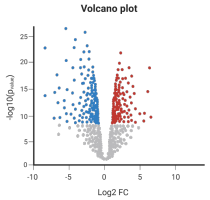
Quantitative mapping (>105,000 phospho-sites covering >10,000 proteins)

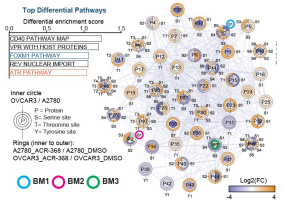




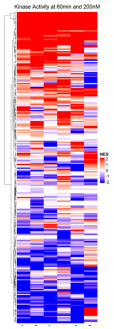
Drug-regulated phospho-sites and biological process enrichment

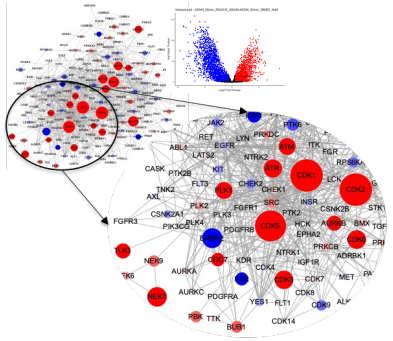


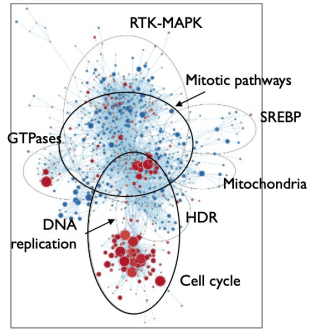




Drug-regulated pathway activity mapping and reconstitution







AP3 enables pathway-based drug design for optimal drug properties

Week 0

Turnaround <2 weeks

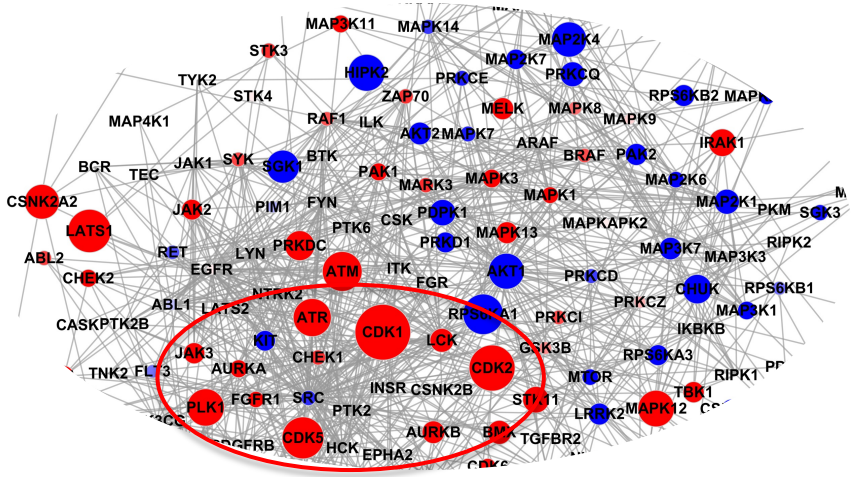
Week 2

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

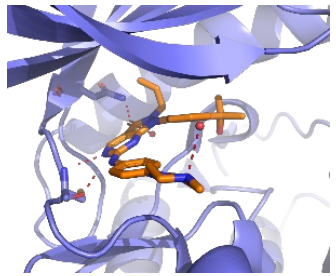
Program goals (superior therapeutic index):

- **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



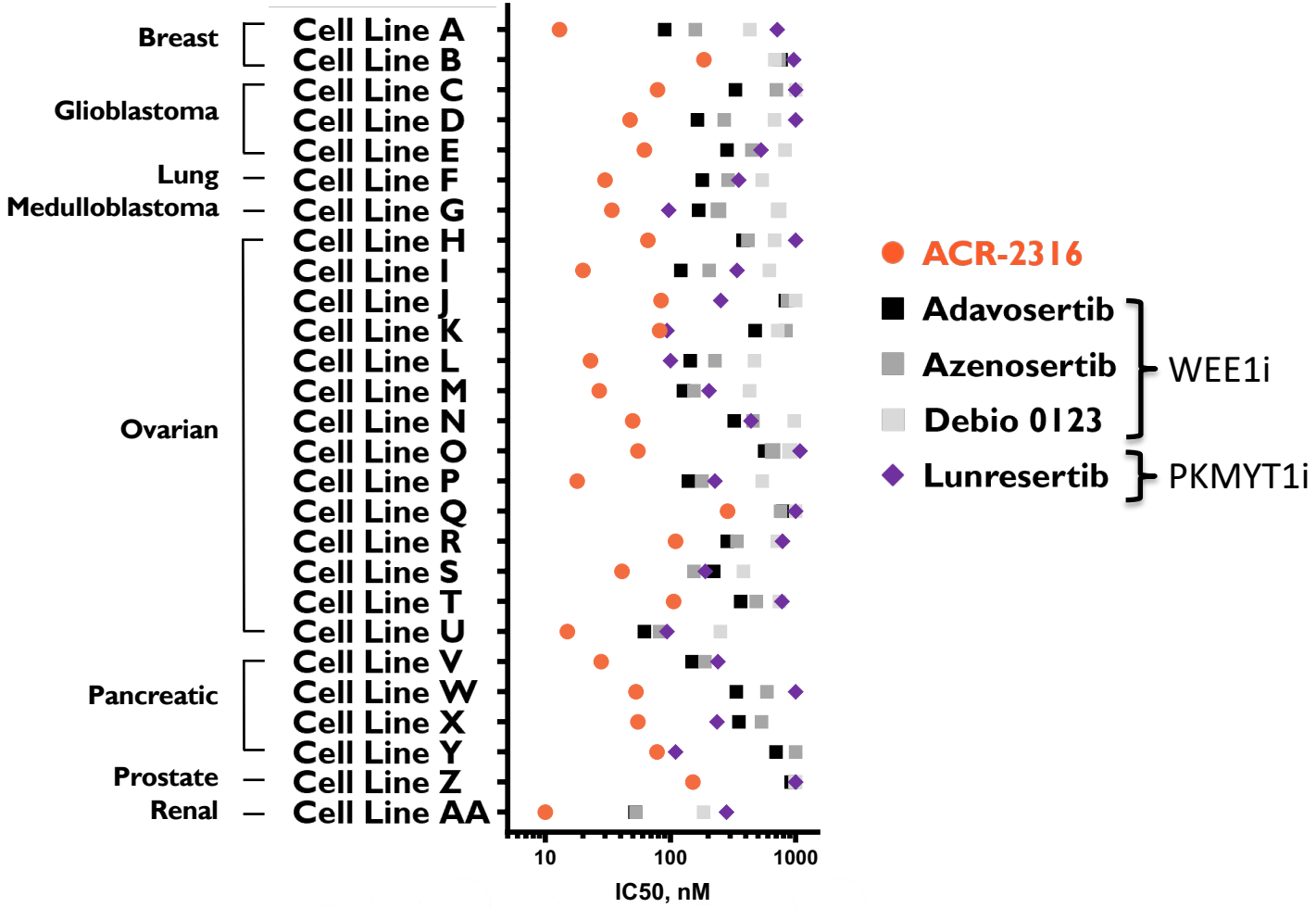
Zhu et al, J. Med. Chem. (2017)

ACR-2316: Rationally designed WEE1/PKMYT1 inhibitor

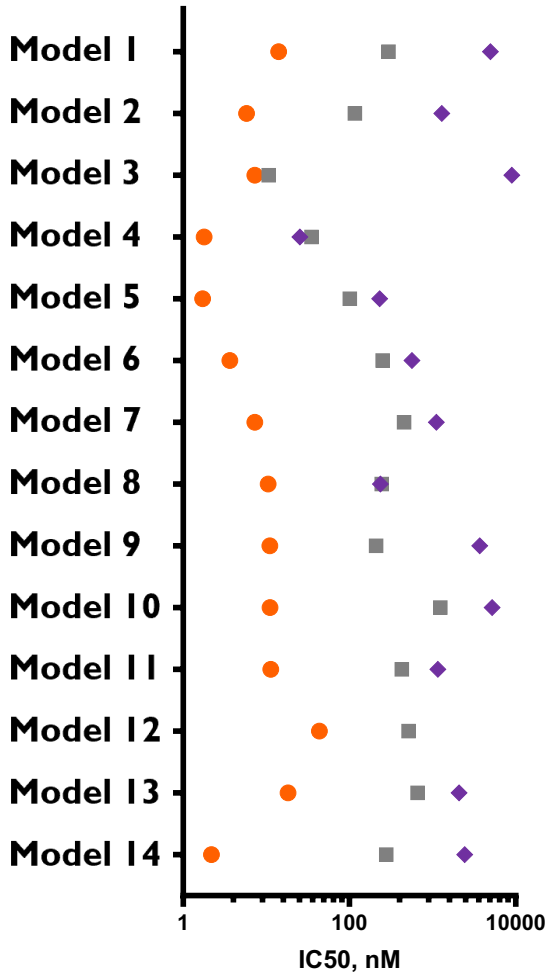
- ✓ Superior anti-tumor efficacy with complete tumor regression across models
- ✓ High selectivity ensures transient, short-lived, mild AEs
- ✓ Potent WEE1 inhibition, balanced PKMYT1 inhibition, overcomes resistance and enables robust activation of CDK1, CDK2, and PLK1 for mitotic catastrophe

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

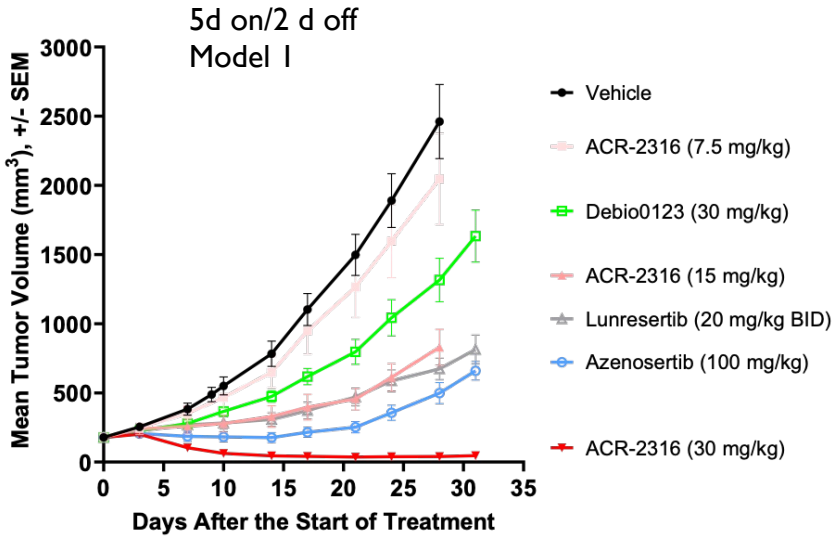
Human tumor cell lines (not genetically selected)

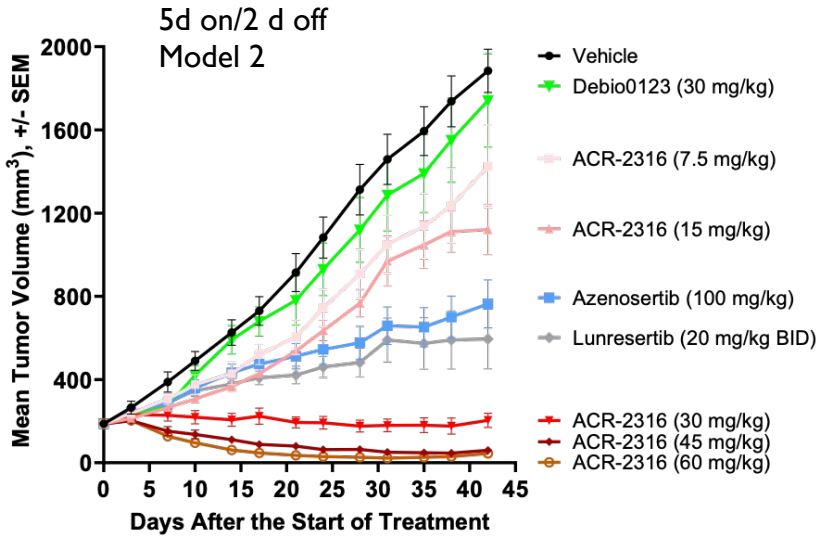


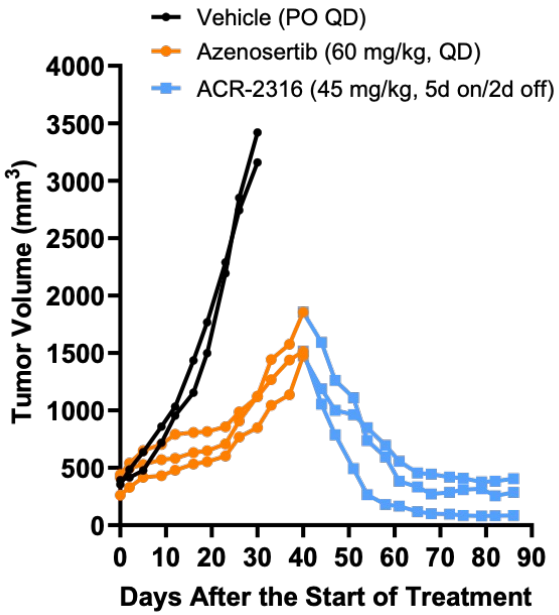
Patient-derived *ex vivo* ovarian tumor models

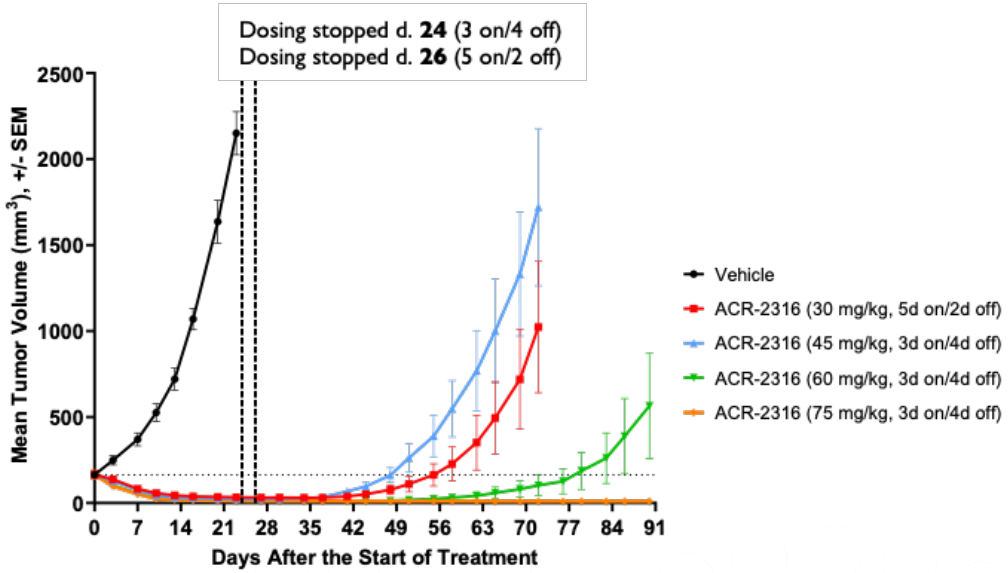


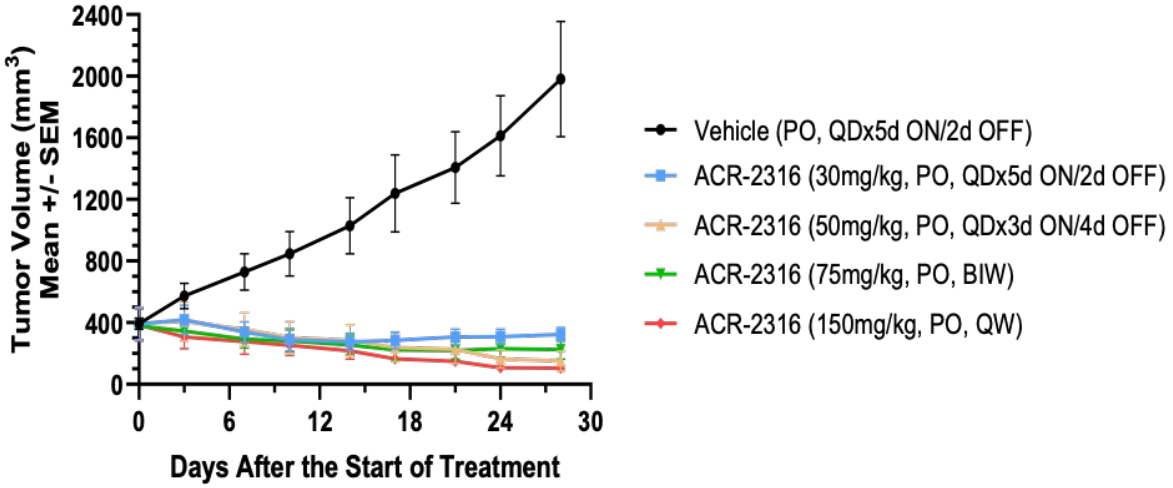
ACR-2316 INDUCES COMPLETE TUMOR REGRESSION ACROSS MODELS AND DOSING REGIMENS











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

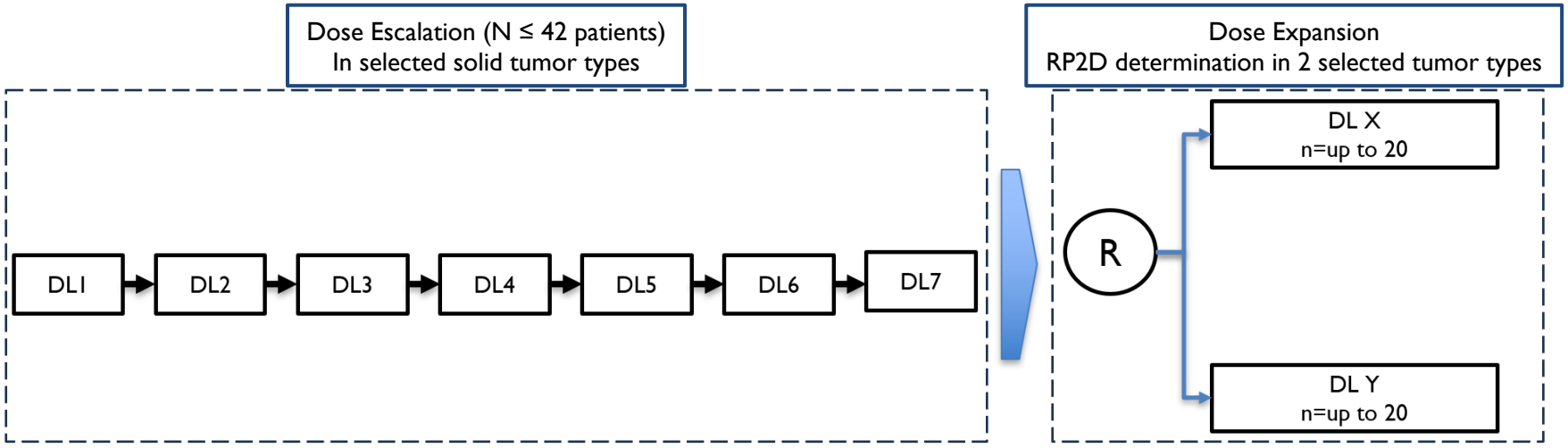
Rat and dog MTD, DRF, and GLP tox studies:

- 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

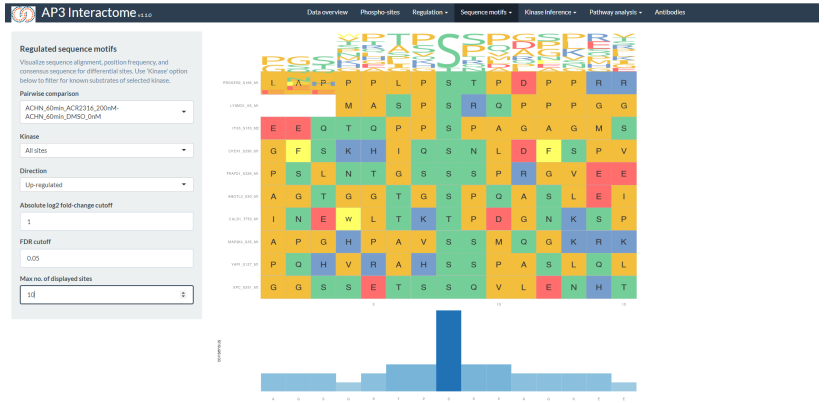
Consensus Sequence Motif

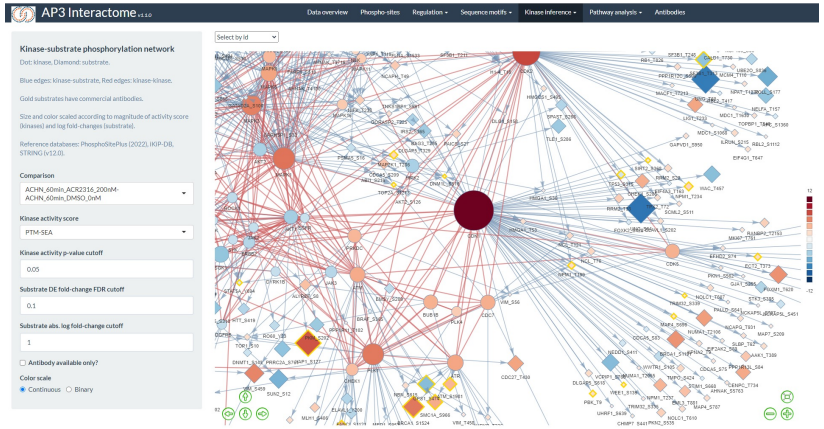
Pathway Enrichment

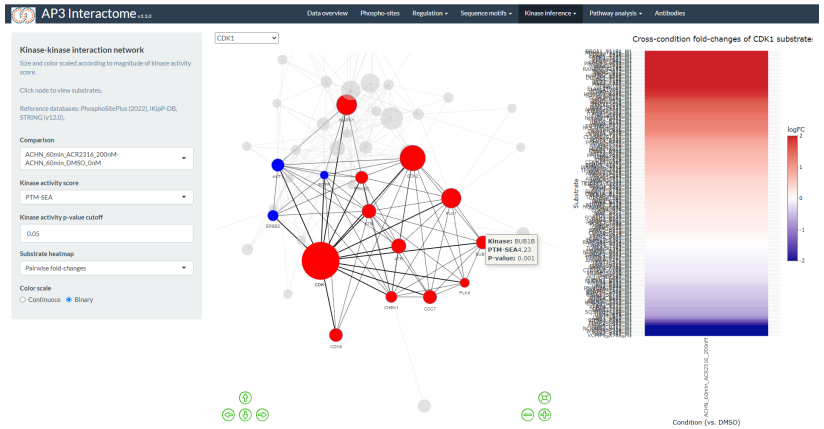
Kinase Inference

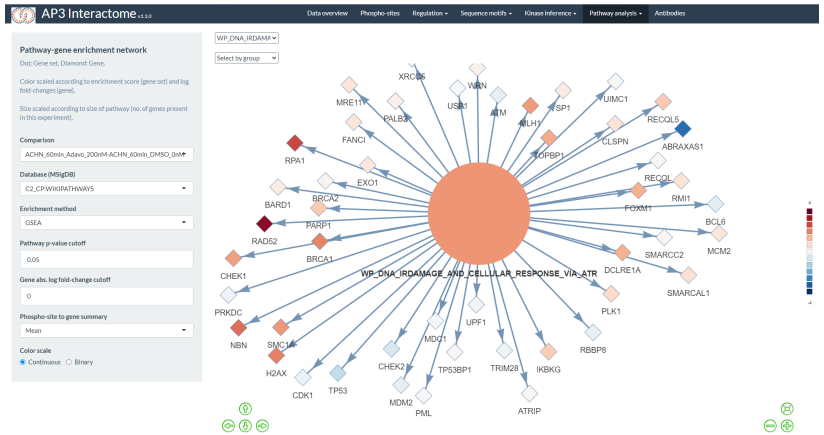
Network Mapping

Biomarkers





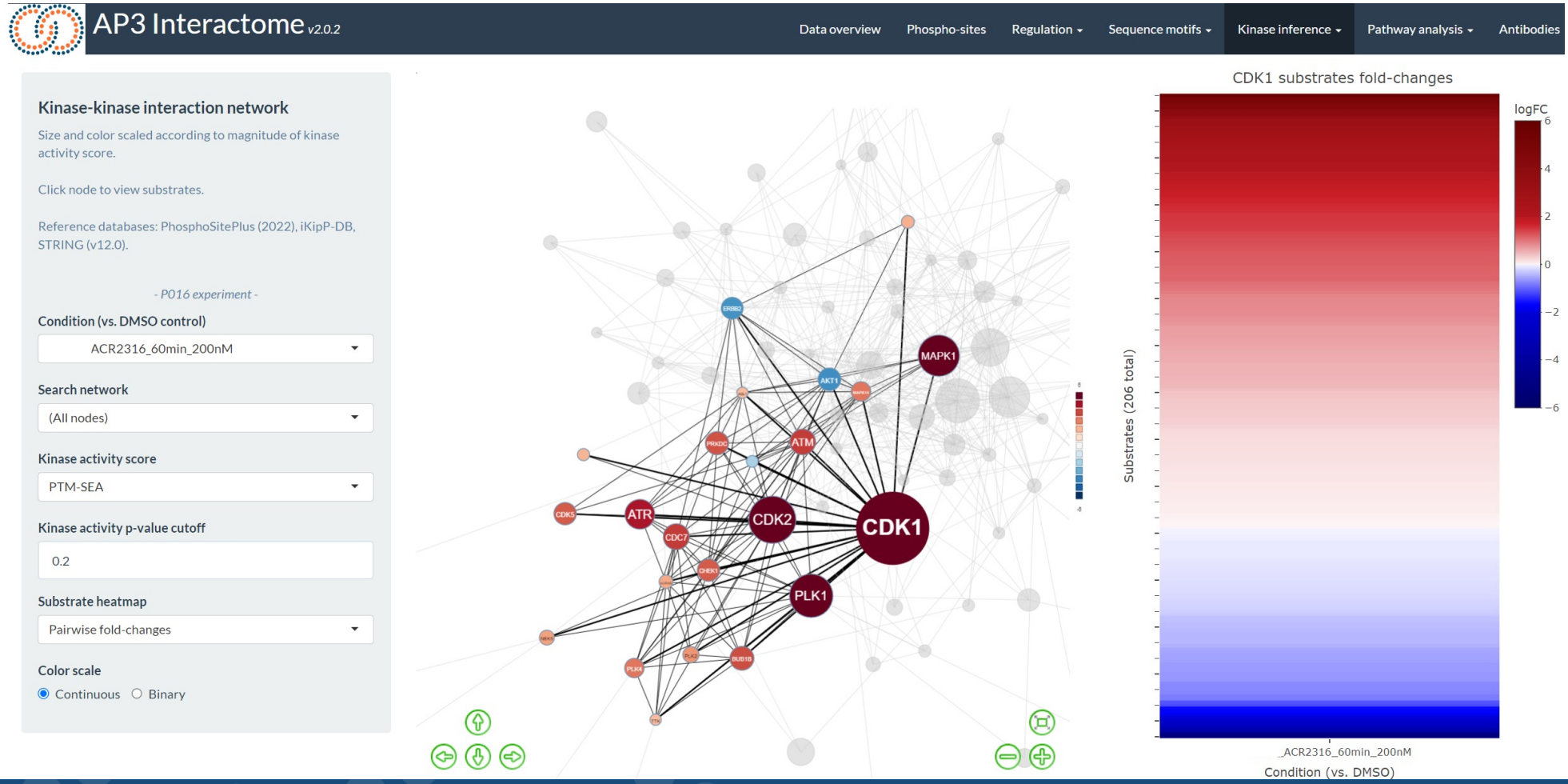




ACR-2316 INDUCES POTENT ACTIVATION OF PRO-APOPTOTIC MITOTIC KINASES IN SENSITIVE TUMOR CELLS

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

ACR-2316 @60min and 200nM in ACHN



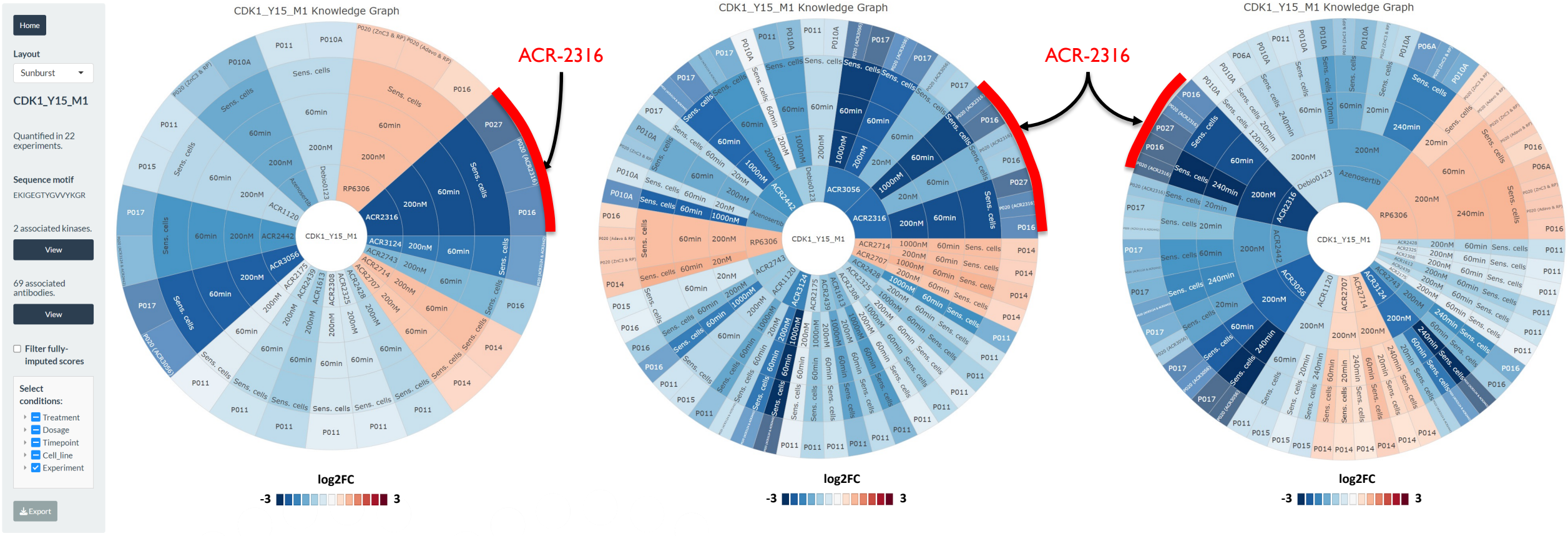
ROBUST POTENT INHIBITION OF CDK1 CONSENSUS SUBSTRATE Y15 BY ACR-2316

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

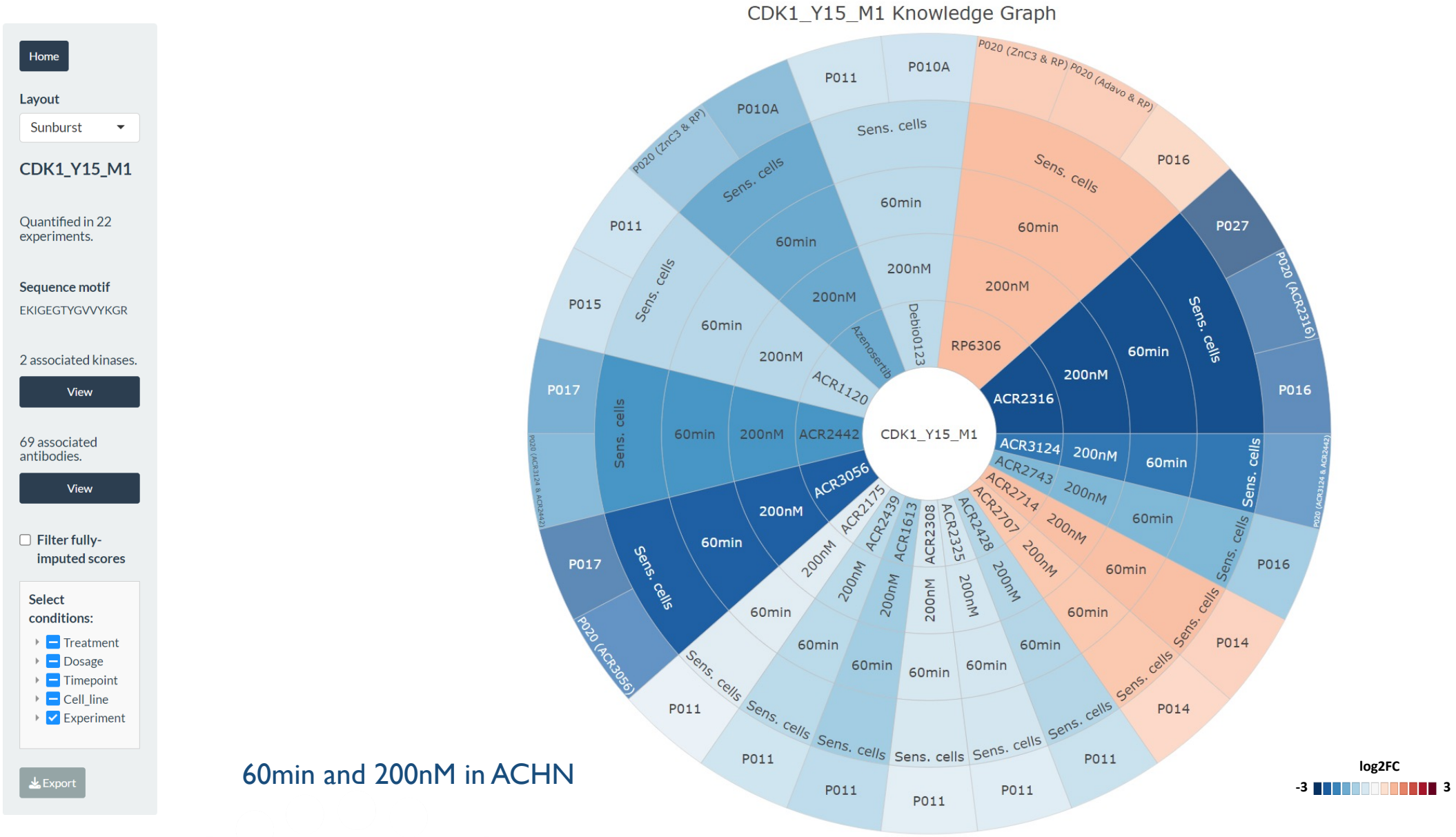
Comparison
@60min and 200nM in ACHN

Dose-dependent comparison
@ 60min in ACHN

Time-dependent comparison
@ 200nM in ACHN



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

Home

Layout

Sunburst

CDK1_Y15_M1

Quantified in 22 experiments.

Sequence motif

EKIGEGTYGVVYKGR

2 associated kinases.

View

69 associated antibodies.

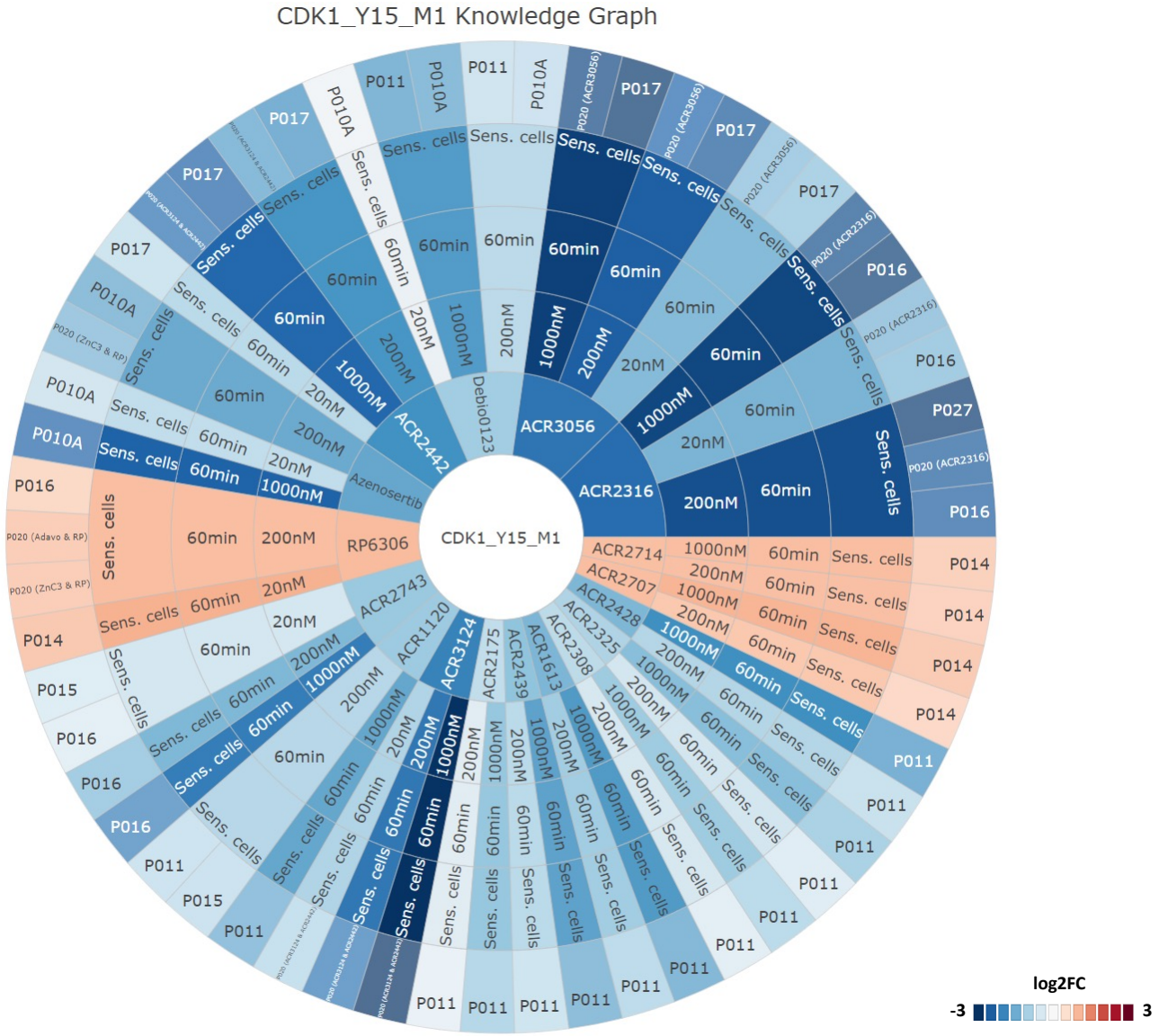
View

Filter fully-imputed scores

Select conditions:

- Treatment
- Dosage
- Timepoint
- Cell_line
- Experiment

Export



Dose-dependent comparison @ 60min in ACHN

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

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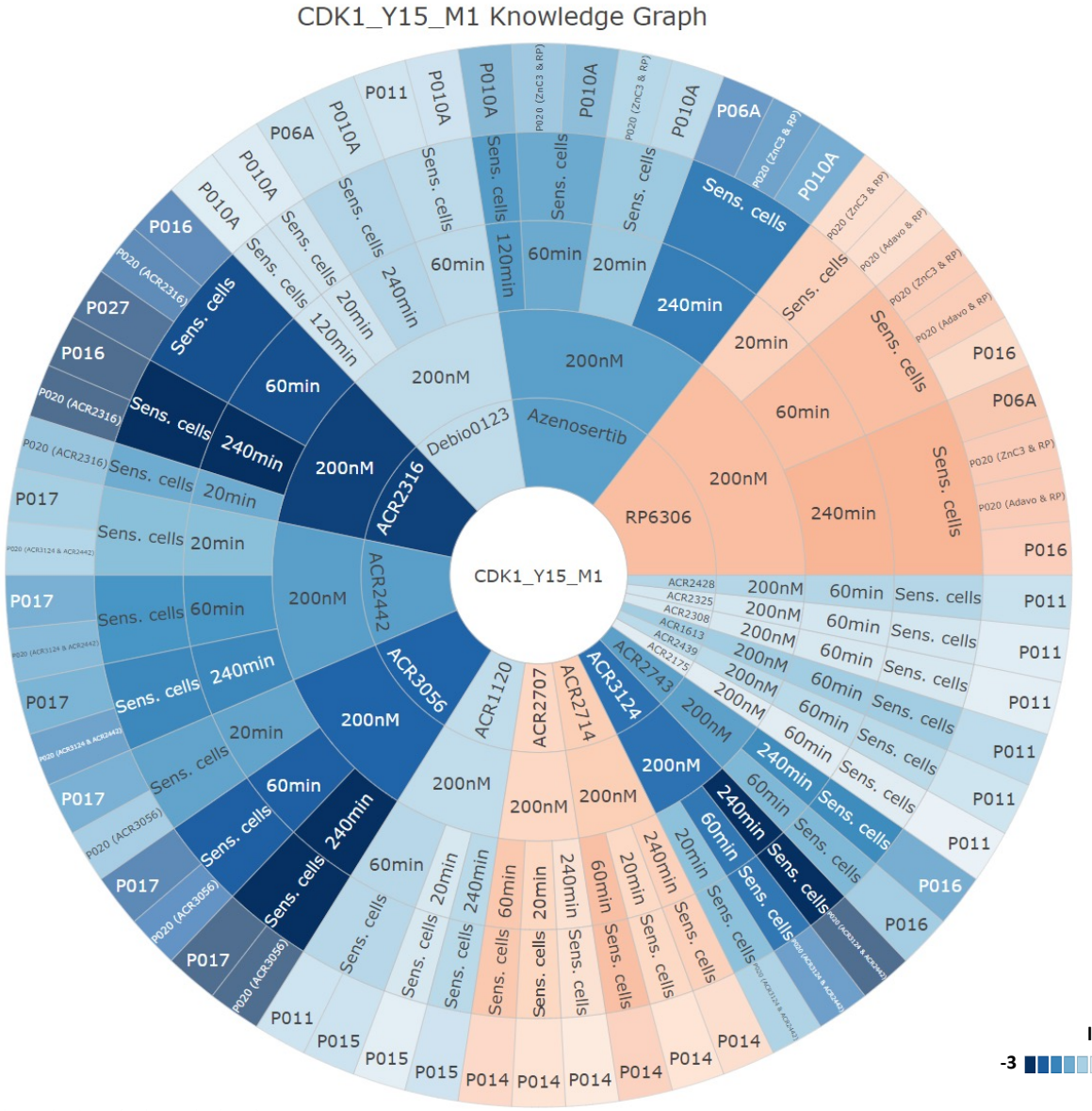
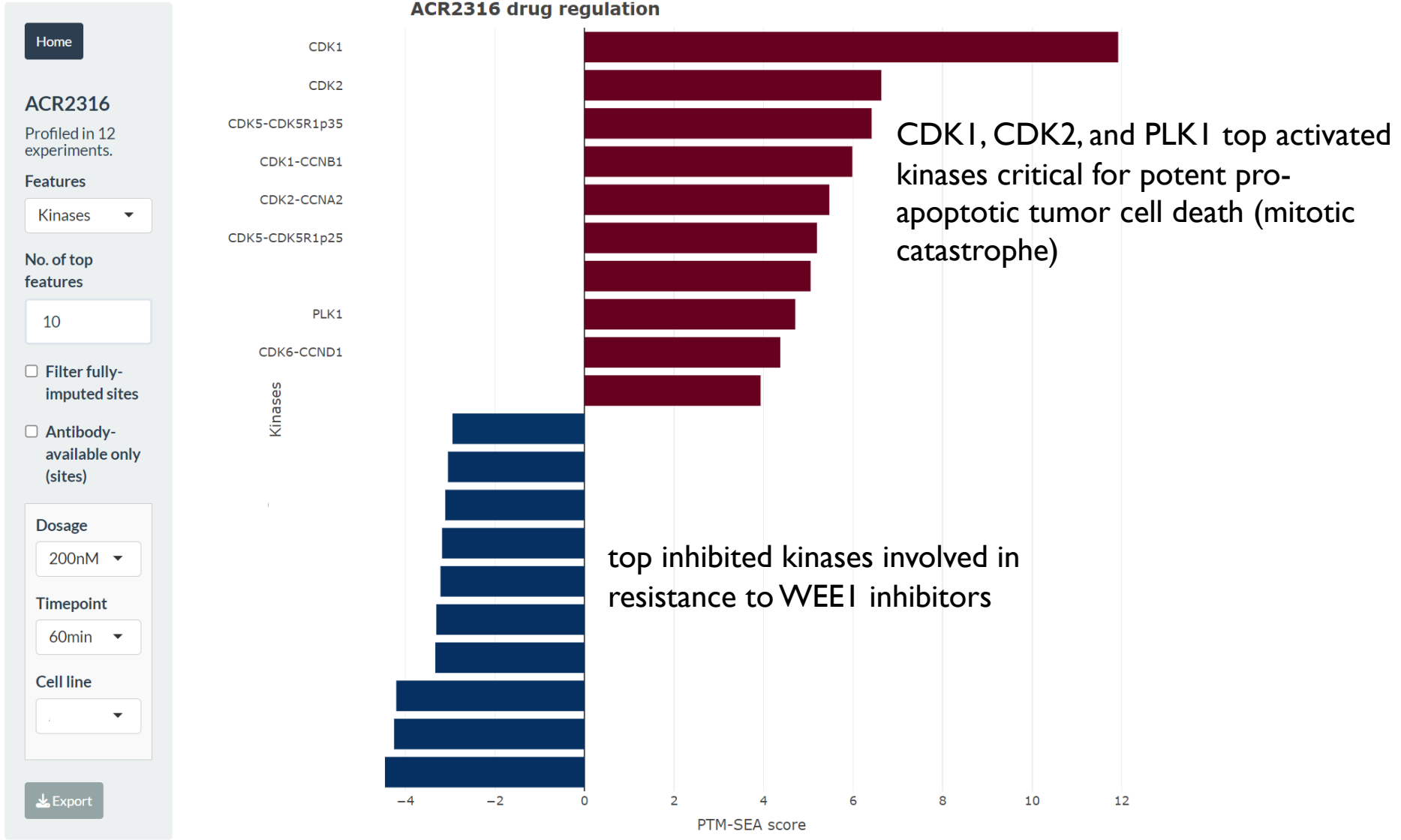


Time-dependent comparison @ 200 nM in ACHN

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

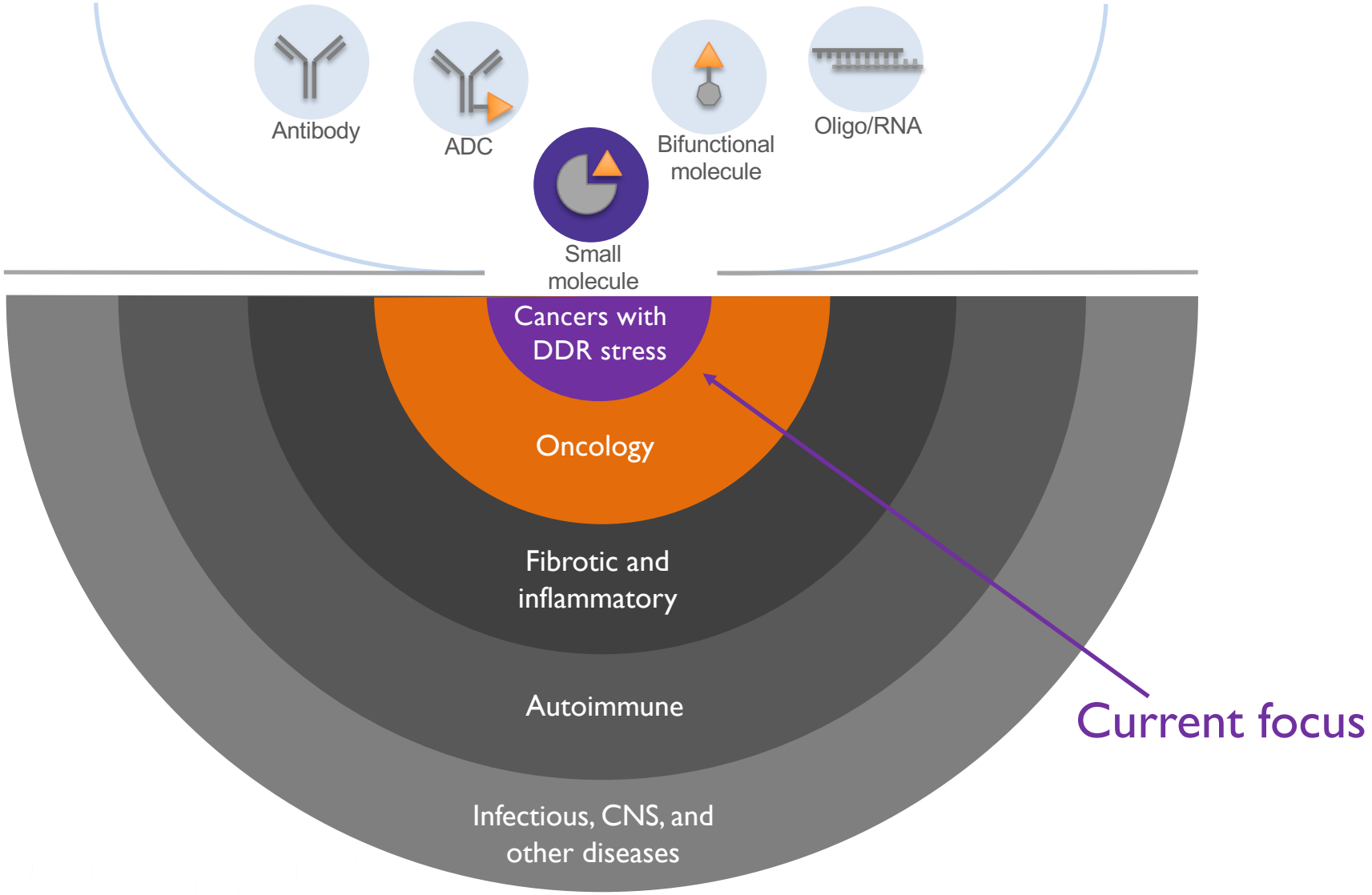
1. Interim registrational intent Phase 2 clinical data for ACR-368 endometrial cancer cohort*, with confirmed ORR (63%) and lower bound of confidence interval (~30%), solidifying endometrial cancer as likely first indication for potential approval
2. Statistically significant segregation of responders 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

Therapeutic modalities

Therapeutic areas



- **Q&A session**