Acrivon Therapeutics

ACRIVON PREDICTIVE PRECISION PROTEOMICS (AP3)

OVERCOMING LIMITATIONS OF GENETICS-BASED PRECISION MEDICINE

CORPORATE PRESENTATION

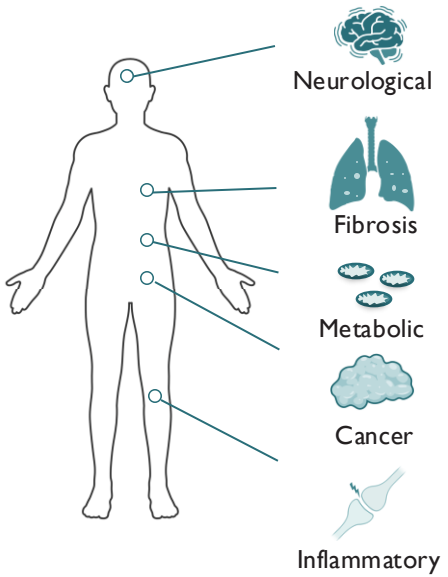
JANUARY 2025

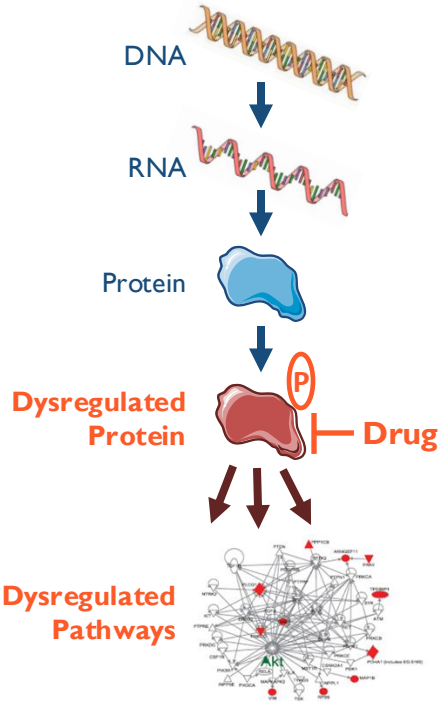
FORWARD-LOOKING STATEMENTS

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.

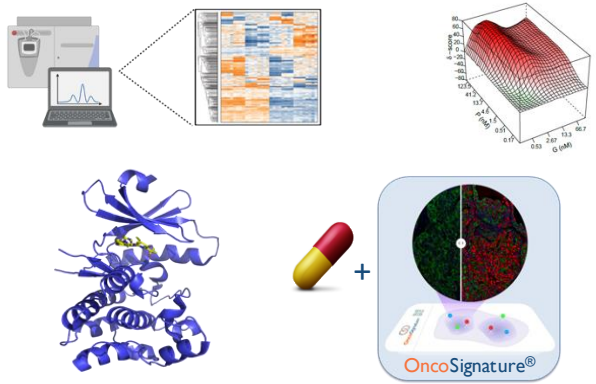
ACRIVON THERAPEUTICS – A NEXT-GENERATION PRECISION MEDICINE COMPANY





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)

ACRIVON THERAPEUTICS FOUNDATION

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

Precision-Proteomics Site (Lund/Copenhagen)
- **Early pipeline drug programs**
- **BM identification and drug profiling**
- **Mass spectrometry**

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

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
Novo-Nordisk Foundation
Protein Center, Cph.
Academic Co-Founder.

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

Founded 2018, IPO November 2022 (NASDAQ:ACRV)

For more information, please visit https://acrivon.com

ACCOMPLISHED LEADERSHIP TEAM

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

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

Rasmus Holm-Jorgensen
Chief Financial Officer

- Novo Nordisk Finance and IR
- Synageva pipeline expansion and $9bn sale to Alexion
- Kiniksa founding team, IPO and commercial launch

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)

Jean-Marie Cuillerot, M.D.
Chief Medical Officer

- Chief Medical Officer, Agenus, Dragonfly
- Global head of clinical development in immuno-oncology at EMD Serono
- Clinical development leadership roles at BMS and Novartis

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

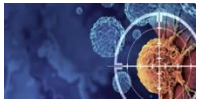
Erick Gamelin, M.D., Ph.D.
Chief Development Officer

- Professor, CEO, large national cancer center and hospital
- Executive Amgen, Pfizer, Dynavax, MacroGenics; CMO STEP Pharma
- >100 ph 1-3 oncology trials

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

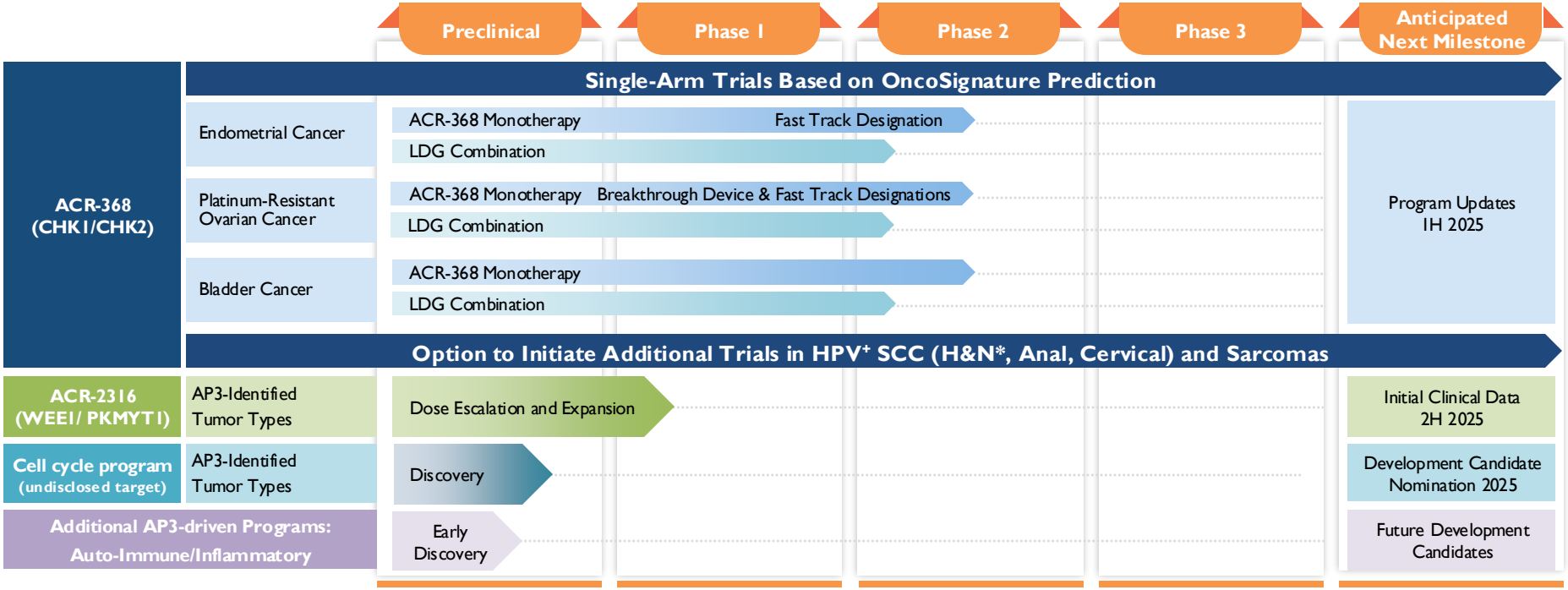
- Over 20 years corporate legal experience
- Served as general counsel of 2 companies taken public
- Boston Business Journal "40 Under 40"

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

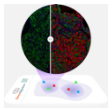
ACRIVON PIPELINE



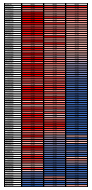
ACR-368 Monotherapy	Registrational intent Phase 2 single arm trials based on predicted sensitivity to ACR-368 monotherapy in OncoSignature-positive patients
LDG Combination	Exploratory Phase 1b/2 single arm trials of ACR-368 in combination with low dose gemcitabine, or LDG, in OncoSignature-negative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

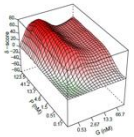
*Investigator-Initiated Trial (IIT) activated at Moffitt Cancer Center

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

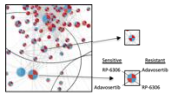
Resistance Mechanisms
Rational drug combinations

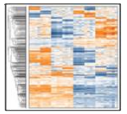
AP3

Drug Discovery SAR
Optimal target selectivity

PD Markers
~40,000 per compound

Informs in-licensing
AP3 profiling of candidates





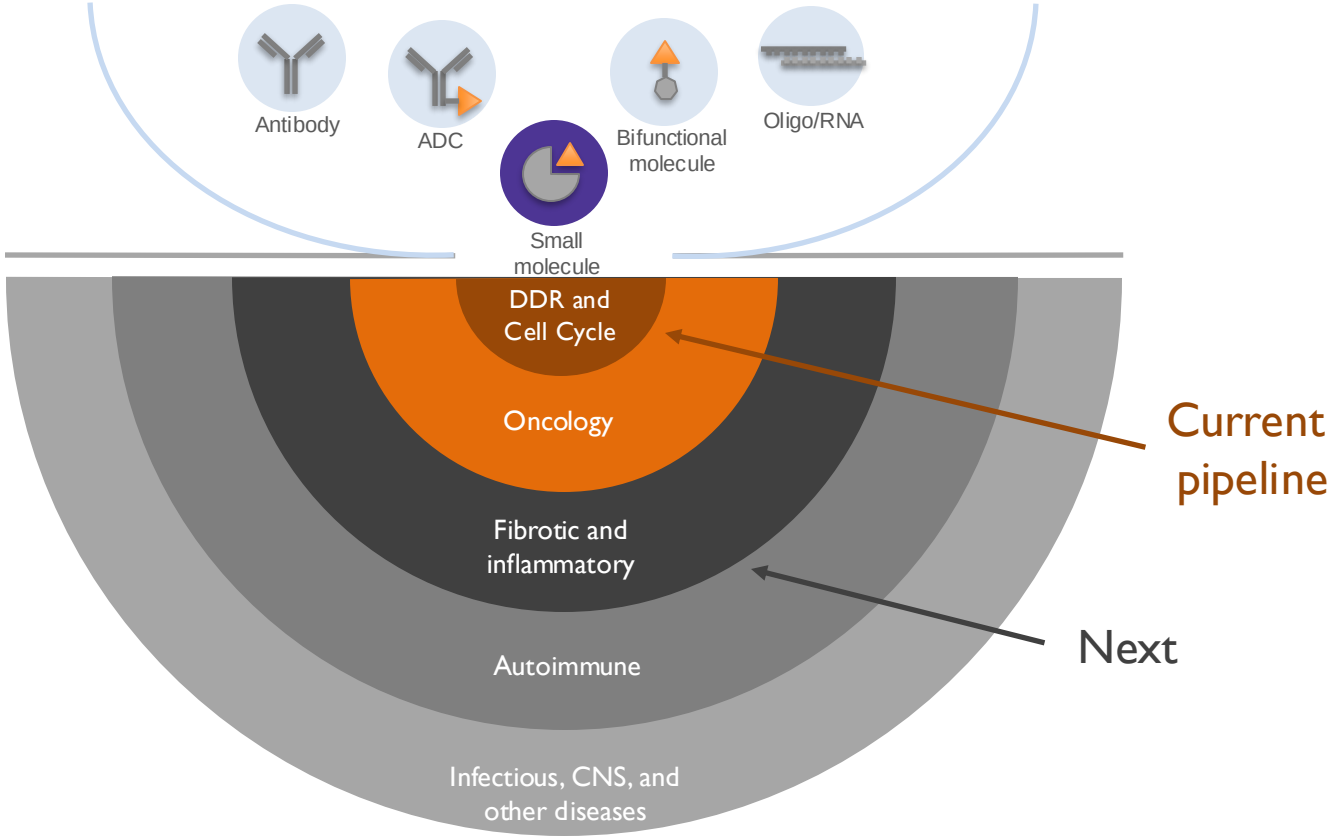
Streamlined Clinical Development
Predicted sensitive indications with informed dose optimization

Predicted Responder

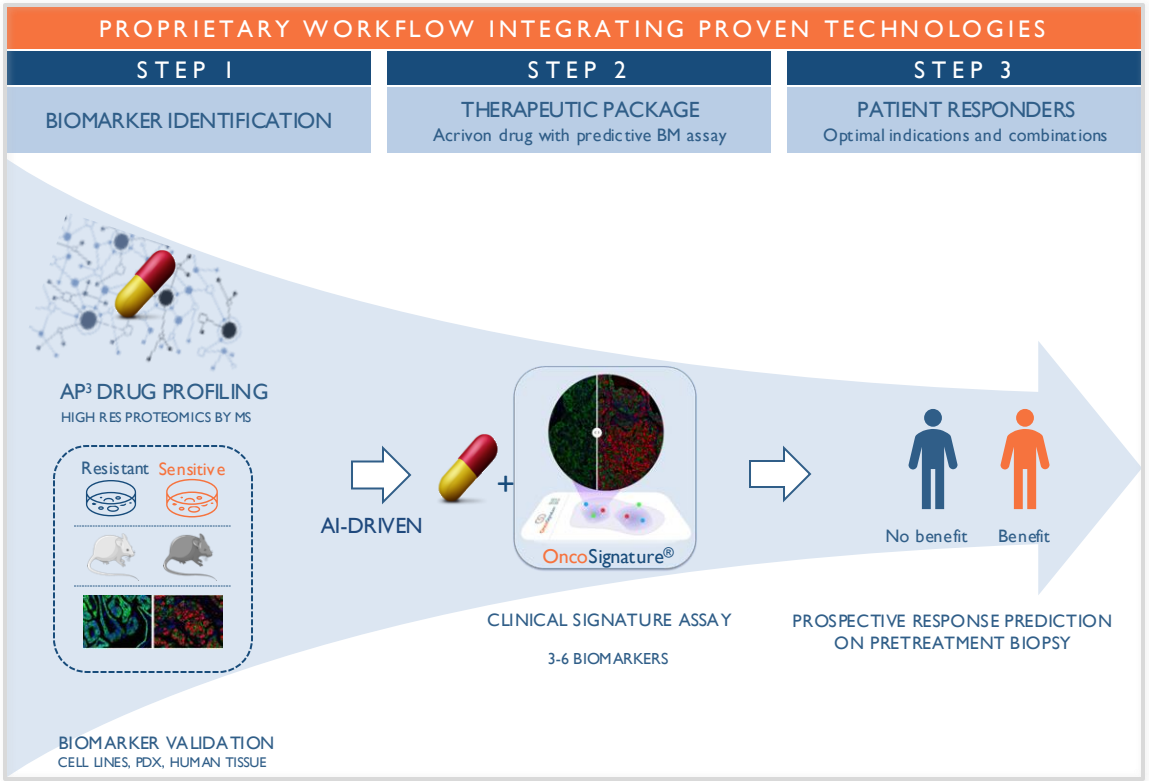
THE AP3 APPROACH IS MODALITY AND DISEASE AGNOSTIC

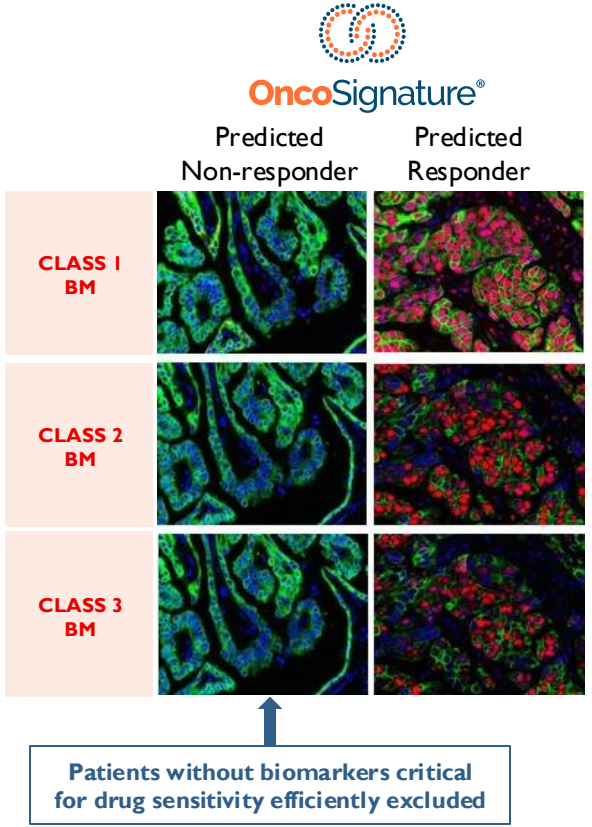
Therapeutic modalities

Therapeutic areas



AP3 PLATFORM: DRUG RESPONSE PREDICTION IN INDIVIDUAL PATIENTS

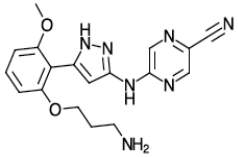




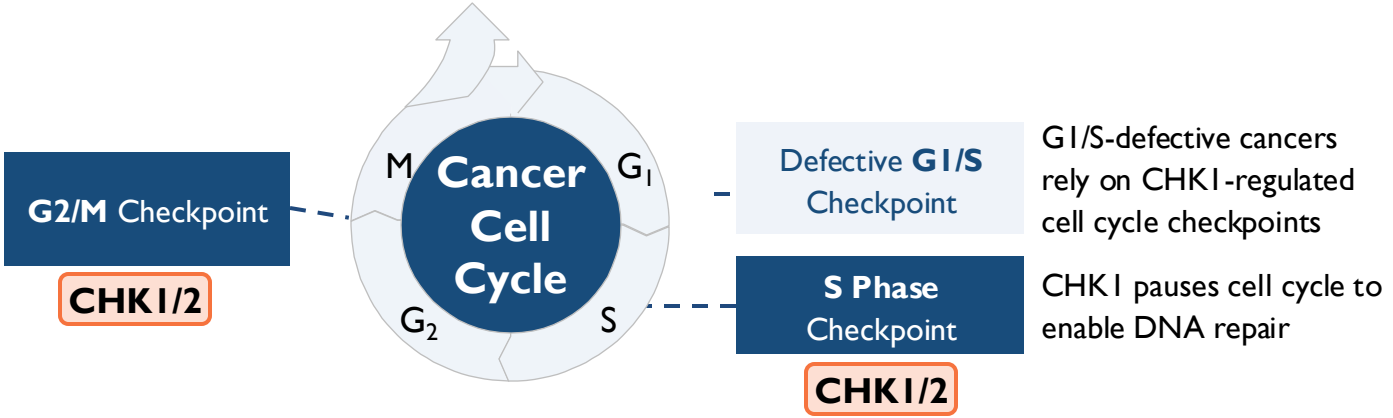
"Disease Pathway-Based Method to Generate Biomarker Panels Tailored to Specific Therapeutics for Individualized Treatments": EP 2 229 589, issued June 10, 2015; US2017/0067877A9, pending. OncoSignature® *is a Registered Trademark: US Reg. No. 5,718,472; Int. Cl. 5, 42. Intl. Reg. 1382289*

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

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



ACR-368 (MW): 365.4



DRUG TARGET PROFILE AT TIME OF IN-LICENSING

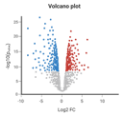
- **Durable monotherapy activity:** Platinum-resistant ovarian and squamous cell cancers (Anal and H&N)
- **Large safety database, favorable safety profile:** >1,000 patients treated (~50% mono, ~50% in combination)
- **Ideal for AP3 method:** Proven clinical activity, but requires patient responder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

DEVELOPMENT OF AP3-BASED PATIENT SELECTION ONCOSIGNATURE TESTS

P-proteomics

Quantitative mapping up to ~105,000 p-sites; 25% drug-related

Drug-regulated phospho-sites and biological processes



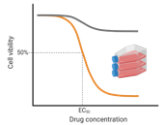
Pathway visualization and reconstitution

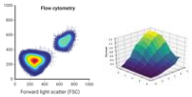
Literature and database mining

Initial biomarker candidates

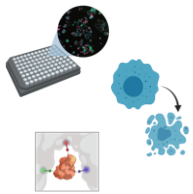
Cellular MOA

Dose response, knockdowns, drug combinations



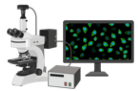


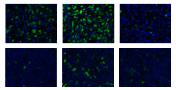
Target engagement, cell assays, imaging

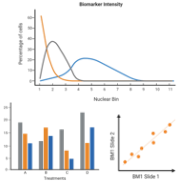


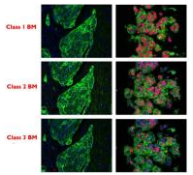
Technical Validation (Intended use tissue)

BM antibody validation by quantitative IF on human and PDX samples

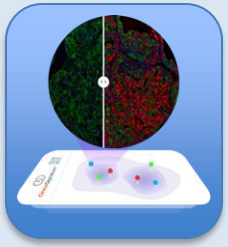








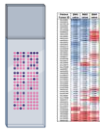
Final OncoSignature Assay



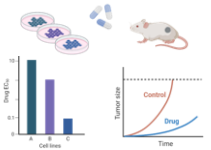
OncoSignature®

Functional Validation (Intended use tissue)

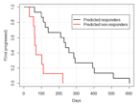
Human cancer screening: ID of drug-sensitive cancers and proportions of responders



Prediction of drug sensitivity in cancer cell lines and PDX models

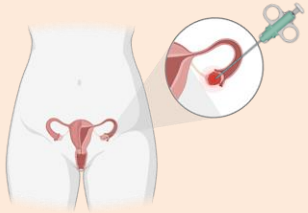


Patient responder prediction on pre-treatment tumor biopsies

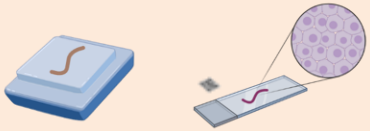


ACR-368 ONCOSIGNATURE TEST: USAGE IN THE CLINIC

Pretreatment tumor biopsy

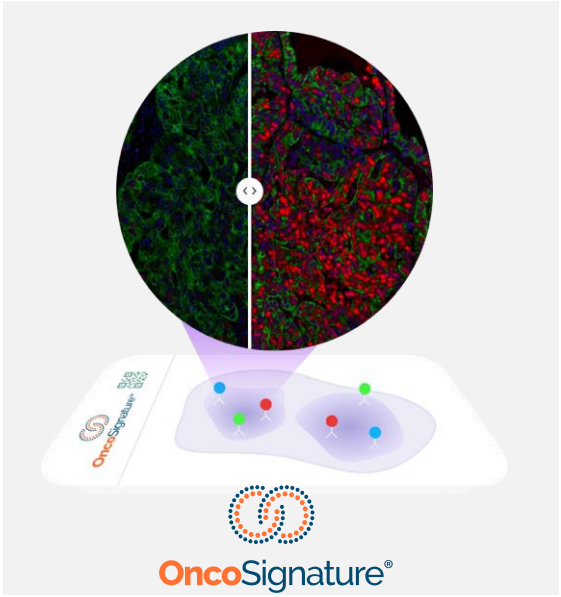


Routine FFPE processing



Biopsy in FFPE block

Automated tumor Region-of-Interest biomarker scoring

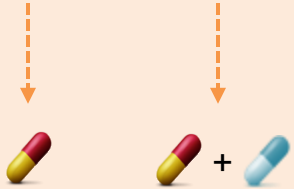


- Pretreatment tumor biopsy test
- Compatible with 5 business days turn-around
- Offered by CDx partner under exclusive license from Acrivon

Treatment decision based on patient stratification

OncoSignature-positive

OncoSignature-negative

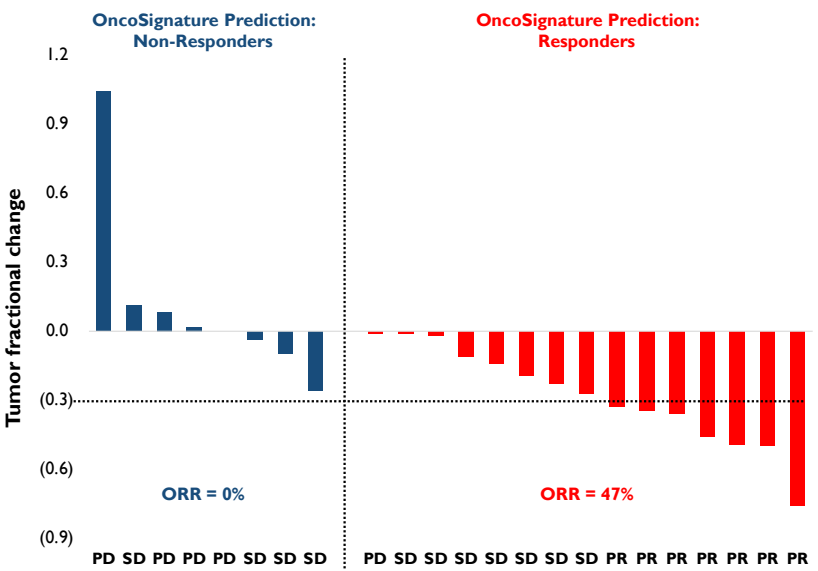


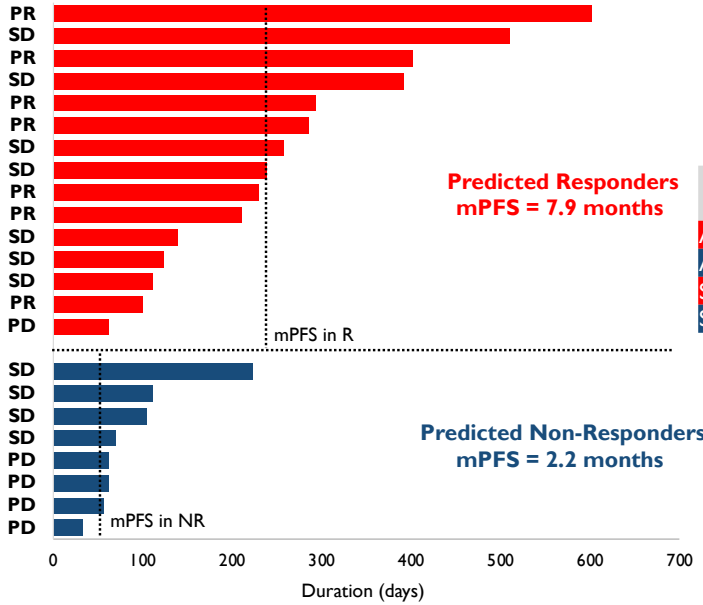
ACR-368 monotherapy

ACR-368 + LDG combination

BIOPSY STUDY 1: SUBSTANTIAL RESPONSE AND PFS BENEFIT IN PREDICTED RESPONDERS (BLINDED, PROSPECTIVELY DESIGNED STUDY)

- Available pretreatment tumor biopsies from past phase 2 trials at NCI with ACR-368 in platinum-resistant ovarian cancer were obtained
- OncoSignature scores were generated **blinded to treatment outcome** at Acrivon and analyzed by **3rd party biostatistician** in **prospectively designed** study





	mPFS (days)
All Predicted R	238.0
All Predicted NR	66.5
SD in predicted R	238.0
SD in predicted NR	108.0

OncoSignature®

Result: ORR ~47%; mPFS = 7.9 months

TWO ADDITIONAL HIGH UNMET NEED SOLID CANCERS PREDICTED ACR-368-SENSITIVE THROUGH HUMAN TUMOR SAMPLE SCREENING

HGS Ovarian

Tissue ID	BM1	BM2	BM3
Fov010719	0.95	0.66	0.78
Fov060075	0.54	0.51	0.38
Fov020069	0.31	0.30	0.38
Fov010899	0.34	0.16	0.36
Fov030970	0.93	0.28	0.33
Fov010892	0.95	0.72	0.32
Fov040102	0.38	0.23	0.29
Fov050734	0.95	0.22	0.25
Fov040164	0.94	0.69	0.21
Fov020776	0.60	0.18	0.19
Fov050764	0.72	0.35	0.17
Fov060380	0.98	0.58	0.17
Fov010172	0.85	0.51	0.17
Fov100051	0.92	0.21	0.16
Fov100142	0.58	0.83	0.14
Fov020160	0.58	0.30	0.14
Fov010252	0.96	0.21	0.14
Fov050617	0.61	0.76	0.14
Fov060302	0.24	0.29	0.13
Fov050836	0.79	0.28	0.13
Fov060050	0.86	0.25	0.12
Fov041285	0.50	0.15	0.11
Fov030109	0.97	0.39	0.10
Fov020386	0.58	0.08	0.09
Fov020067	0.96	0.44	0.08
Fov110030	0.92	0.39	0.08
Fov041267	0.44	0.39	0.06
Fov100004	0.95	0.36	0.05
Fov060083	0.78	0.24	0.05
Fov020061	0.87	0.20	0.05
Fov041269	0.20	0.38	0.04
Fov010873	0.97	0.53	0.03
Fov041300	0.90	0.27	0.03
Fov060152	0.63	0.59	0.02
Fov060265	0.48	0.38	0.02
Fov100146	0.66	0.63	0.01
Fov060382	0.28	0.37	0.01
Fov010706	0.87	0.70	0.01
Fov060133	0.93	0.69	0.01
Fov020059	0.97	0.27	0.01
Fov010682	0.85	0.59	0.01
Fov100220	0.69	0.18	0.00
Fov010750	0.98	0.31	0.00
Fov060434	0.91	0.56	0.00
Fov050840	0.16	0.23	0.00
Fov040044	0.81	0.54	0.00
Fov030062	0.10	0.17	0.00
Fov010563	0.71	0.58	0.00
Fov010903	0.82	0.09	0.00
Fov050139	0.40	0.57	0.00
Fov020762	0.91	0.09	0.00
Fov060553	0.84	0.08	0.00
Fov050417	0.72	0.26	0.00
Fov050855	0.92	0.61	0.00
Fov060371	0.81	0.82	0.00
Fov040694	0.59	0.81	0.00
Fov030128	0.99	0.68	0.00
Fov020497	0.83	0.59	0.00
Fov050700	0.37	0.25	0.00
Fov060210	0.48	0.22	0.00
Fov020106	0.95	0.07	0.11
Fov041138	0.27	0.06	0.03
Fov020002	0.57	0.06	0.08
Fov020111	0.16	0.05	0.11
Fov040872	0.31	0.04	0.01
Fov050666	0.99	0.03	0.00
Fov050659	0.81	0.03	0.00
1176BC3	0.44	0.03	0.05
Fov050555	0.20	0.02	0.01
Fov020193	0.69	0.02	0.00
Fov031530	0.81	0.01	0.10
Fov030763	0.59	0.01	0.29
Fov021215	0.52	0.01	0.07
Fov040855	0.11	0.01	0.04
Fov050706	0.12	0.01	0.00
Fov030120	0.70	0.01	0.00
Fov030286	0.10	0.00	0.00
Fov020132	0.03	0.00	0.01
Fov020486	0.03	0.00	0.00
Fov050816	0.03	0.25	0.00
Fov020263	0.01	0.29	0.06
Fov050388	0.01	0.00	0.00
Fov010181	0.00	0.00	0.00
Fov150230	0.00	0.06	0.19

OncoSignature-positive = 30%
(ORR in past trials: 12+% and 29%)

Sq. NSCLC

Tissue ID	BM1	BM2	BM3
Rin020132	0.17	0.26	0.02
Rin010099	0.08	0.06	0.01
Rin020029	0.48	0.28	0.00
Rin020005	0.34	0.06	0.00
Rin010095	0.28	0.02	0.00
Rin020051	0.11	0.01	0.14
Rin010167	0.14	0.00	0.00
Rin020284	0.09	0.00	0.00
Rin020141	0.05	0.18	0.00
Rin020032	0.05	0.01	0.00
Rin010199	0.05	0.06	0.03
Rin020197	0.04	0.00	0.00
Rin020250	0.04	0.00	0.00
Rin020190	0.04	0.00	0.00
Rin020243	0.02	0.00	0.01
Rin020012	0.02	0.41	0.07
Rin010148	0.02	0.05	0.06
Rin020006	0.01	0.00	0.02
Rin020296	0.01	0.00	0.00
Rin020186	0.01	0.02	0.02
Rin020166	0.01	0.05	0.01
Rin020208	0.01	0.01	0.00
Rin020327	0.01	0.00	0.00
Rin020343	0.01	0.00	0.01
Rin020233	0.01	0.04	0.06
Rin020007	0.00	0.26	0.00
Rin020138	0.00	0.01	0.01
Rin020321	0.00	0.00	0.01
Rin020231	0.00	0.00	0.01
Rin020088	0.00	0.00	0.00
Rin020169	0.00	0.16	0.00
Rin020164	0.00	0.00	0.00
Rin030301	0.00	0.18	0.00
Rin020083	0.00	0.00	0.00
Rin020086	0.00	0.00	0.00
Rin020160	0.00	0.00	0.00
Rin020096	0.00	0.00	0.00
Rin020140	0.00	0.00	0.00
Rin020302	0.00	0.00	0.00
Rin020253	0.00	0.00	0.00
Rin020331	0.00	0.00	0.08
Rin020002	0.00	0.00	0.00
Rin020415	0.00	0.00	0.00
Rin020298	0.00	0.00	0.00
Rin010086	0.00	0.00	0.00
Rin020361	0.00	0.11	0.00
Rin020383	0.00	0.01	0.06
Rin020386	0.00	0.03	0.00
Rin020248	0.00	0.00	0.00
Rin020221	0.00	0.00	0.00
Rin020184	0.00	0.00	0.01
Rin010119	0.00	0.00	0.05
Rin020380	0.00	0.00	0.02
Rin020244	0.00	0.00	0.00
Rin020324	0.00	0.00	0.00
Rin010122	0.00	0.00	0.00
Rin010079	0.00	0.03	0.00
Rin020282	0.00	0.00	0.00
Rin020249	0.00	0.00	0.00
Rin020255	0.00	0.00	0.00

OncoSignature-positive = 0%
(ORR in past trial: 0%)

Bladder cancer

Tissue ID	BM1	BM2	BM3
Ubd040512	0.99	0.48	0.65
Ubd040016	0.30	0.58	0.63
Ubd040039	0.43	0.33	0.54
Ubd030040	0.88	0.73	0.45
Ubd040287	0.63	0.34	0.40
Ubd040151	0.65	0.72	0.34
Ubd040225	0.76	0.64	0.33
Ubd040282	0.27	0.16	0.26
Ubd060279	0.29	0.13	0.16
Ubd030229	0.79	0.39	0.15
Ubd040104	0.84	0.58	0.15
Ubd040056	0.79	0.83	0.14
Ubd070017	0.62	0.40	0.14
Ubd040204	0.12	0.76	0.12
Ubd040131	0.95	0.81	0.10
Ubd040142	0.84	0.62	0.09
Ubd030138	0.54	0.11	0.09
Ubd040043	0.65	0.92	0.08
Ubd050077	0.72	0.46	0.08
Ubd020464	0.73	0.63	0.07
Ubd040177	0.89	0.84	0.04
Ubd040214	0.29	0.17	0.03
Ubd040128	0.77	0.29	0.03
Ubd050035	0.17	0.33	0.02
Ubd080024	0.18	0.28	0.01
Ubd040101	0.26	0.31	0.01
Ubd030151	0.79	0.61	0.00
Ubd040098	0.35	0.40	0.00
Ubd040008	0.75	0.90	0.00
Ubd040162	0.97	0.10	0.00
Ubd040341	0.19	0.09	0.03
Ubd070027	0.20	0.08	0.01
Ubd040030	0.95	0.07	0.01
Ubd040067	0.81	0.06	0.03
Ubd040074	0.60	0.03	0.10
Ubd040213	0.85	0.02	0.15
Ubd040055	0.07	0.03	0.02
Ubd040050	0.06	0.58	0.00
Ubd020068	0.05	0.11	0.18
Ubd040144	0.03	0.57	0.00
Ubd040242	0.00	0.05	0.00
Ubd040256	0.00	0.17	0.01

OncoSignature-positive = 30-50%

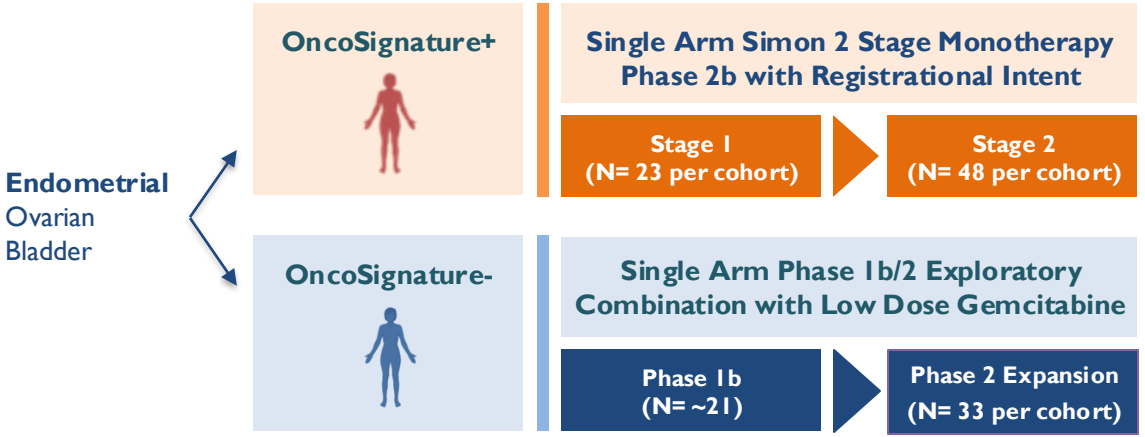
Endometrial cancer

Tissue ID	BM1	BM2	BM3
Fur021904	0.16	0.38	0.86
Fur021989	0.86	0.17	0.71
Fur021785	0.14	0.55	0.69
Fur021984	0.87	0.62	0.63
Fur021937	0.81	0.65	0.61
Fur022037	0.12	0.22	0.54
Fur130035	0.55	0.48	0.50
Fur030113	0.90	0.65	0.31
Fur020288	0.60	0.26	0.30
Fur020281	0.21	0.57	0.27
Fur130010	0.79	0.75	0.27
Fur021781	0.75	0.31	0.26
Fur140135	0.72	0.35	0.25
Fur150643	0.61	0.73	0.22
Fur021558	0.61	0.33	0.22
Fur020131	0.73	0.57	0.18
Fur021367	0.30	0.55	0.18
Fur020506	0.94	0.68	0.17
Fur020163	0.23	0.33	0.12
Fur130009	0.18	0.69	0.10
Fur021197	0.35	0.70	0.09
Fur010587	0.18	0.34	0.08
Fur140260	0.77	0.51	0.07
Fur021980	0.30	0.70	0.06
Fur020831	0.18	0.45	0.04
Fur020809	0.36	0.58	0.00
Fur030068	0.41	0.63	0.00
Fur030131	0.50	0.68	0.00
Fur021437	0.98	0.37	0.00
Fur021620	0.41	0.10	0.33
Fur020073	0.29	0.06	0.21
Fur020115	0.56	0.02	0.00
Fur020107	0.68	0.00	0.17
Fur020703	0.05	0.27	0.00
Fur021233	0.05	0.66	0.00
Fur021561	0.04	0.01	0.14
Fur020837	0.04	0.06	0.04
Fur020266	0.04	0.40	0.03
Fur020280	0.03	0.42	0.25
Fur030193	0.03	0.10	0.02
Fur021641	0.02	0.30	0.01
Fur020121	0.02	0.14	0.01
Fur030025	0.01	0.03	0.01
Fur021248	0.01	0.32	0.05
Fur021721	0.01	0.35	0.00
Fur021423	0.01	0.35	0.04
Fur020604	0.01	0.02	0.00
Fur020155	0.01	0.09	0.07
Fur020408	0.01	0.39	0.02
Fur020821	0.00	0.22	0.08
Fur030114	0.00	0.73	0.00
Fur021562	0.00	0.07	0.00
Fur020786	0.00	0.00	0.00
Fur021353	0.00	0.00	0.00
Fur021216	0.00	0.21	0.04
Fur021372	0.00	0.08	0.40
Fur021334	0.00	0.04	0.01
Fur021642	0.00	0.38	0.01
Fur021075	0.00	0.19	0.07

OncoSignature-positive = 30-40%

ENROLLING AND DOSING ACR-368 IN THREE HIGH UNMET NEED INDICATIONS: ENDOMETRIAL, OVARIAN, AND BLADDER CANCER

- ACR-368 dosed at RP2D based on prospective response prediction using the ACR-368 OncoSignature Assay run by our CDx partner
- 68 sites activated[1]
- OB-GYN Key Opinion Leaders actively participating



- FDA Fast Track Designation granted May 8, 2023 for ACR-368 monotherapy in OncoSignature-positive patients with platinum-resistant endometrial cancer and ovarian cancer
- FDA Breakthrough Device Designation granted November 16, 2023 for ACR-368 OncoSignature Assay for the identification of ovarian cancer patients who may benefit from treatment with ACR-368

[1]https://clinicaltrials.gov/ct2/show/NCT05548296

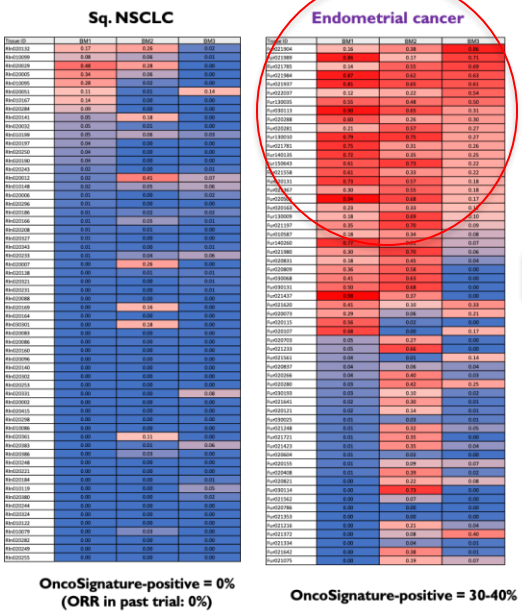
ENDOMETRIAL CANCER IS AN AP3-PREDICTED TUMOR TYPE

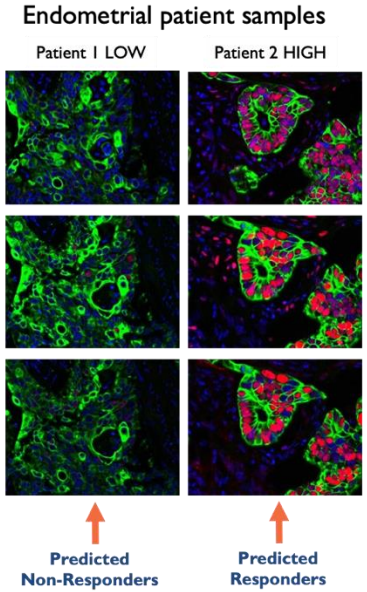
ACR-368 OncoSignature-based indication finding prior to trial entry

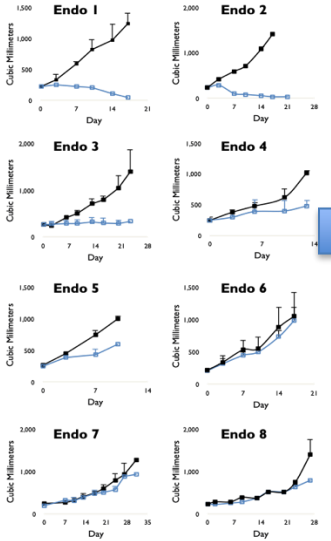
ACR-368 OncoSignature imaging demonstrates addiction to CHK1/2 DDR axis

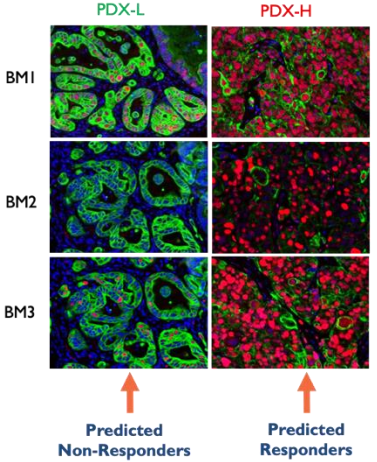
Confirmation of predicted sensitivity in genetically non-modified PDX models

Confirmation of ACR-368 OncoSignature prediction in PDX tumor tissues pretreatment



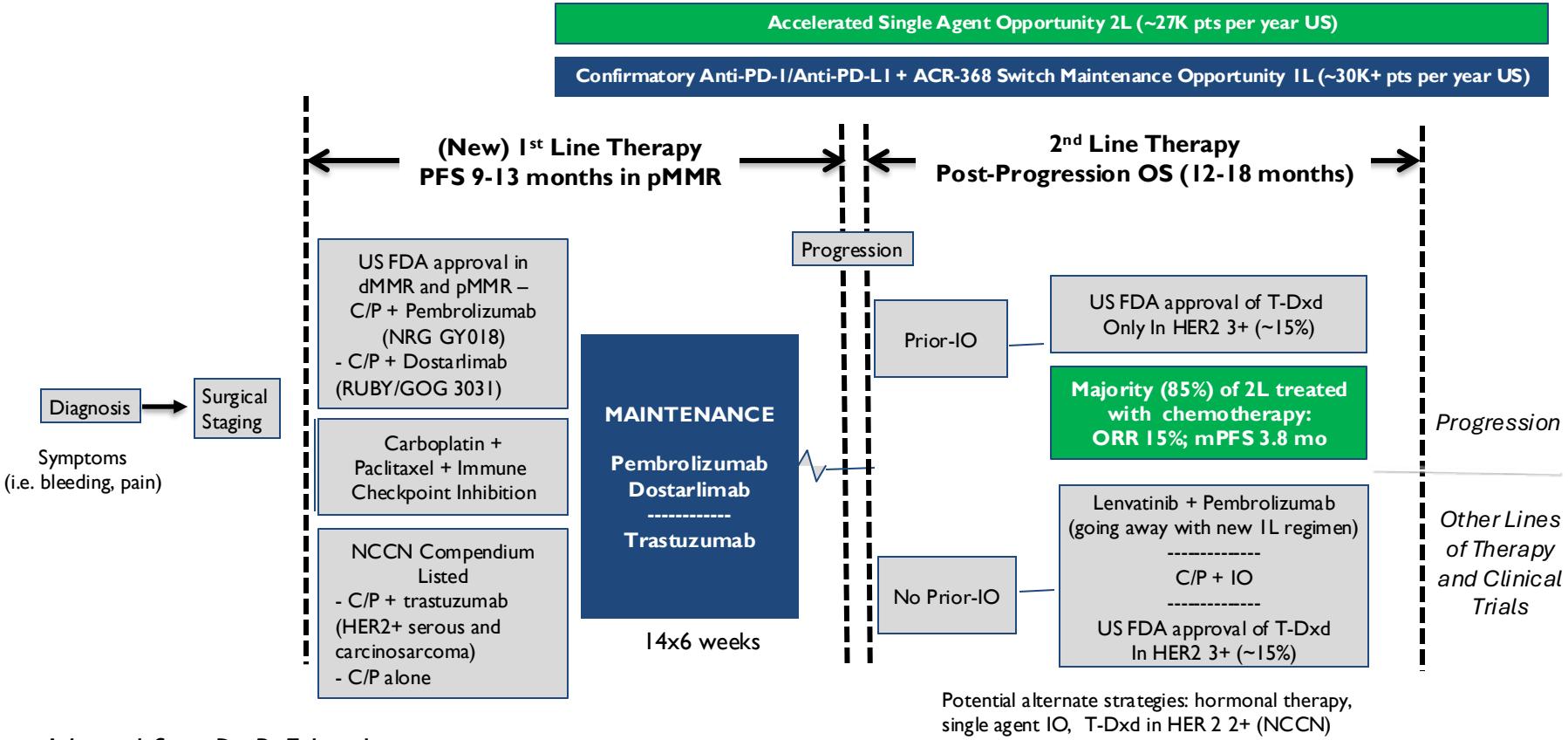






In >1,000 cancer patients treated with ACR-368 in Lilly-sponsored trials, endometrial cancer was not tested

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



Adapted from Dr. R. Eskander

HIGH GRADE ADVANCED STAGE ENDOMETRIAL CANCER

POTENTIAL FOR ACCELERATED APPROVAL ≥ 2ND LINE (POST ANTI-PD-1)

ACR-368 Target Indication

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

SOC:

- ≥2nd line (post-PD-1 + chemo) ~14.7% ORR, mPFS 3.8 months[2]; patients in the control arm were not previously treated with anti-PD-1 therapy, only platinum, thus potentially overestimating the 2nd line ORR
- ≥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

SIGNIFICANT ACR-368 ENDOMETRIAL PATIENT 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)

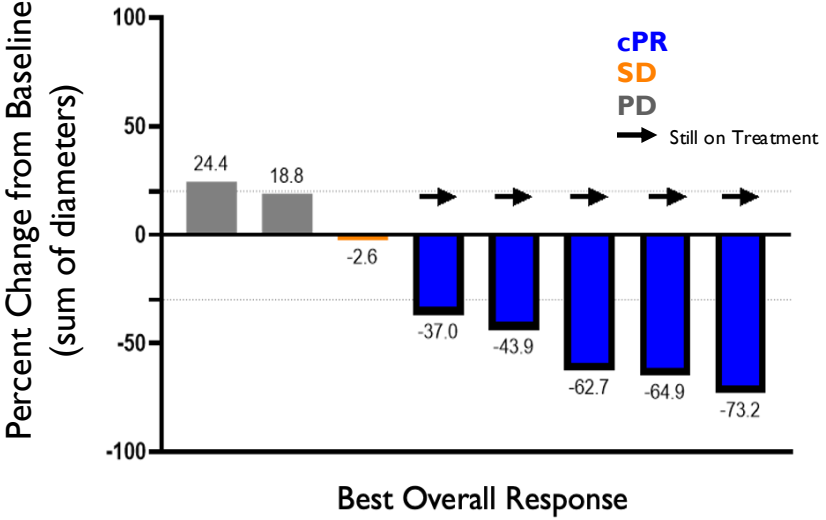
Endometrial Cancer (data cut 25 July 2024)			
Overall Response	**BM+ Monotherapy**	**BM- LDG Combination**	**Total**
	N = 8	N = 15	N=23
	N (%)	N (%)	N (%)
CR	0 (0)	1 (7)	1 (4)
cPR	5 (63)	0 (0)	5 (22)
uPR	0 (0)	1 (7)	1 (4)
SD	1 (13)	6 (40)	7 (30)
PD	2 (25)	7 (47)	9 (39)
cORR (95% CI)	**62.5% (30.4, 86.5)**	**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

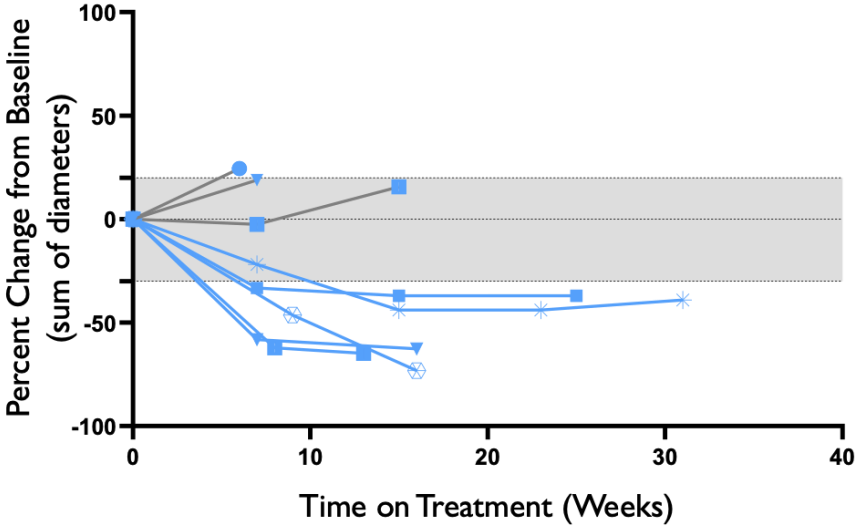
[2]https://ir.acrivon.com/news-events/events-presentations

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

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

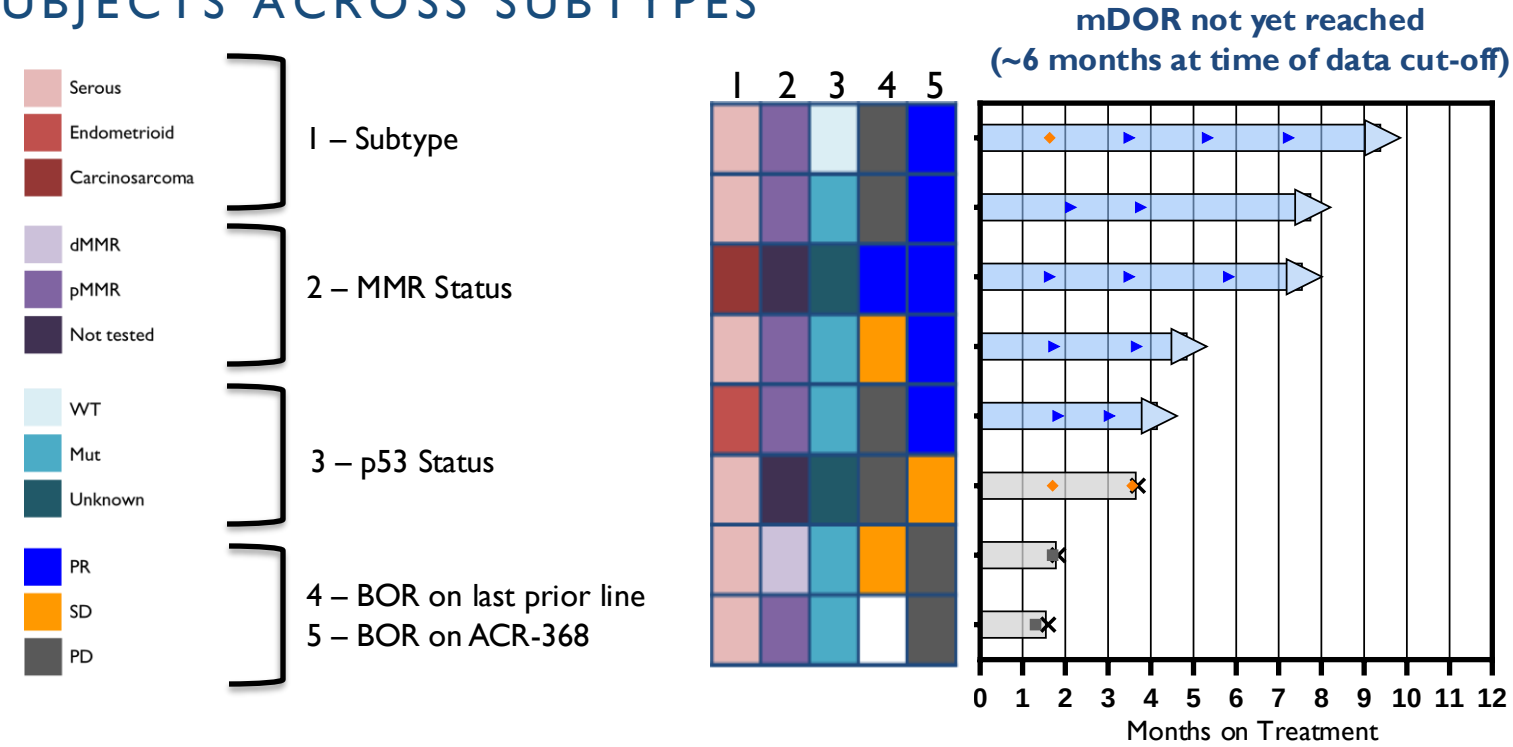


Significant disease control (75%) with most RECIST responses occurring early



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

ONGOING CONFIRMED RESPONSES IN BM+ ENDOMETRIAL 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

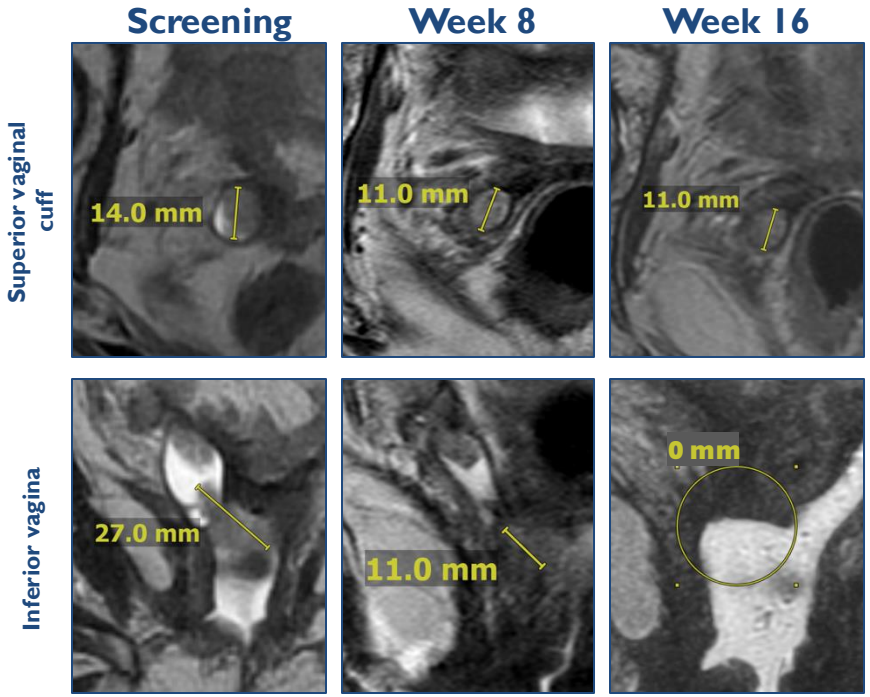
CONFIRMED RESPONSES IN ENDOMETRIAL SUBJECTS WHO ALL PROGRESSED ON PRIOR ANTI-PD-1

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

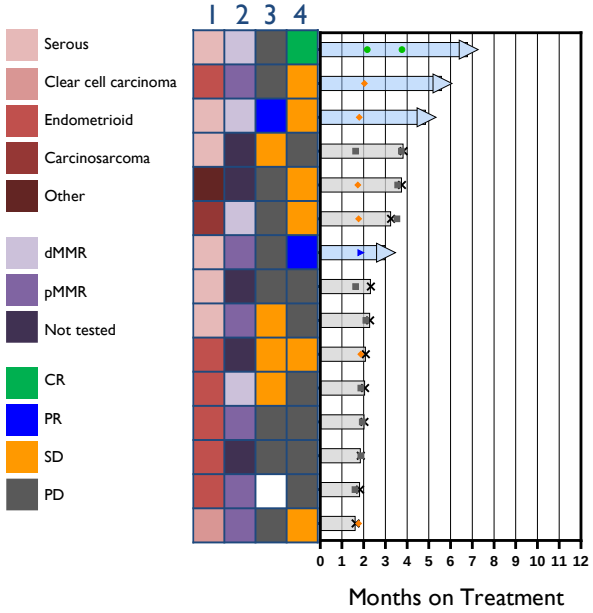
BOR = Best Overall Response, UNK = unknown, NA = not applicable, NT = not tested
Data shown current as of 25Jul2024 and includes all efficacy-evaluable (at least one scan on-treatment) BM+ subjects

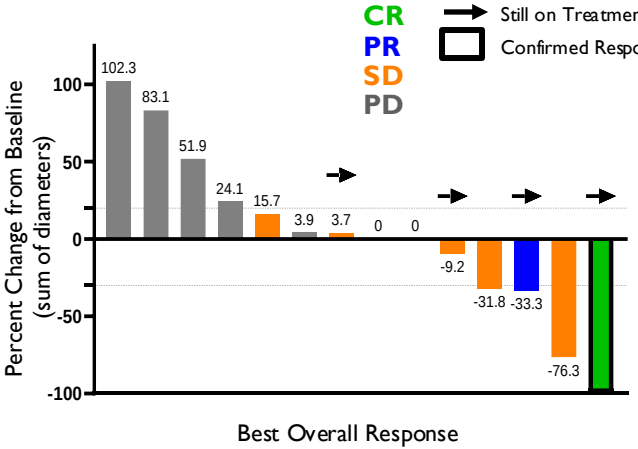
DEEP, RAPID RESPONSES SEEN IN PATIENTS WITH LARGE TUMOR LESIONS

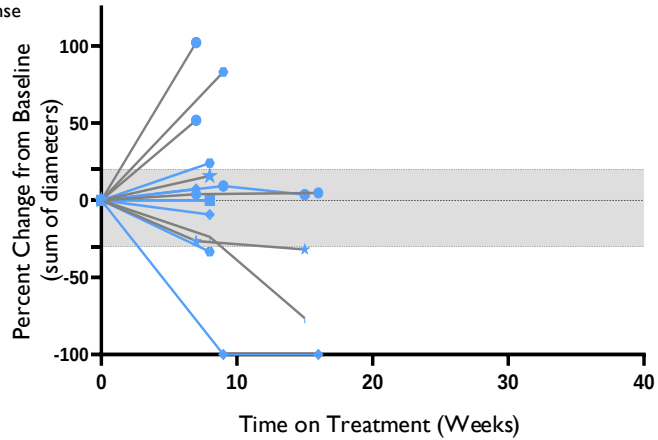


- 72-yo female with Stage III serous endometrial carcinoma (pMMR)
- PD on last prior line (pembrolizumab/lenvatinib)
- Confirmed PR at Week 16
- 73% overall decrease in sum of target lesions from baseline

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







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

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

ENCOURAGING SAFETY PROFILE IN ENDOMETRIAL SUBJECTS

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

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

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

DEVELOPMENT PATH FOR ACR-368 IN ENDOMETRIAL CANCER

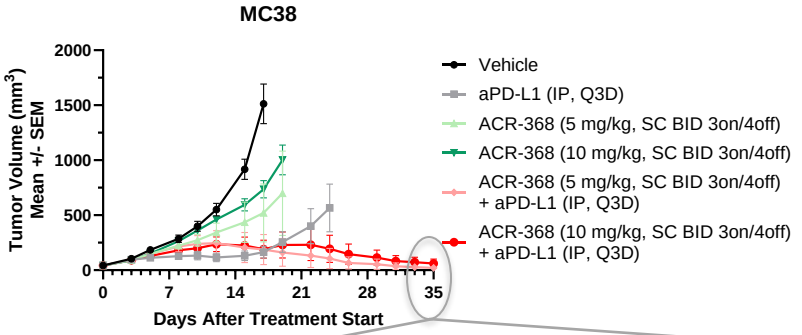
- Accelerated approval pathway
  - Ongoing single arm registrational intent Phase 2 monotherapy endometrial cancer trial represents the first potential approval opportunity for ACR-368

- Confirmatory trial strategy
  - Evaluating options to potentially move towards new front line setting
    - Randomization anti-PD-1 vs [anti-PD-1/anti-PD-L1 + 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, clinical safety data on ACR-368 + anti-PD-1, and strong rationale and preclinical data demonstrating additive/synergistic activity of ACR-368 and anti-PD-1 (Refs: Do KT et al, Cancer Immunol Immunother, 2021; Lyer et al, Cancer Disc 2021; McGrail et al, Sci Transl Med 2021; Sen et al, Cancer Disc 2019)

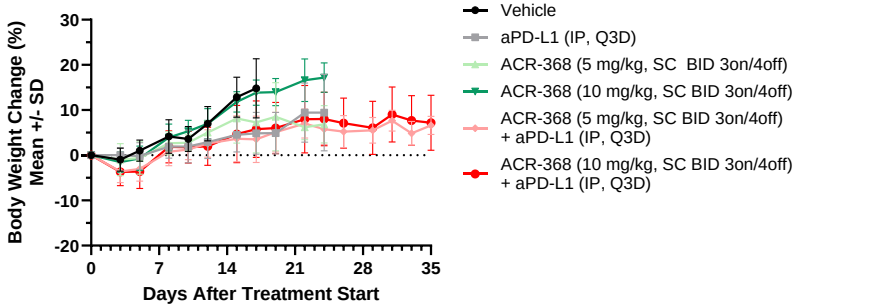
POTENT SYNERGY OF ACR-368 WITH ANTI-PD-L1 IN MC38 SYNGENEIC MOUSE TUMOR MODEL (DEEP PR'S AND CR'S)

Tumor Volume

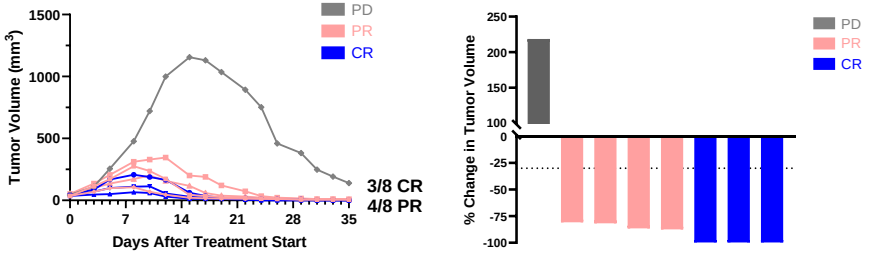


Average TV at start of treatment 43 mm³

Body Weight Change

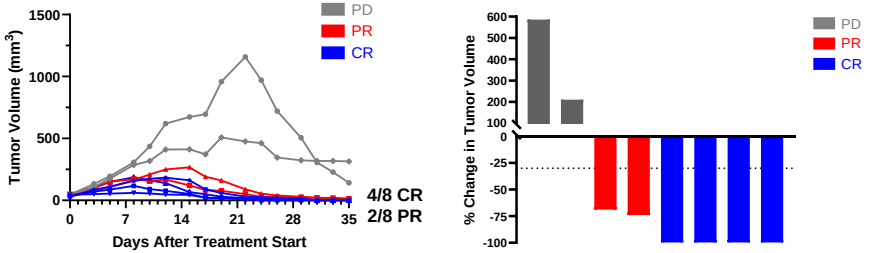


ACR-368 (5 mg/kg) + anti-PD-L1



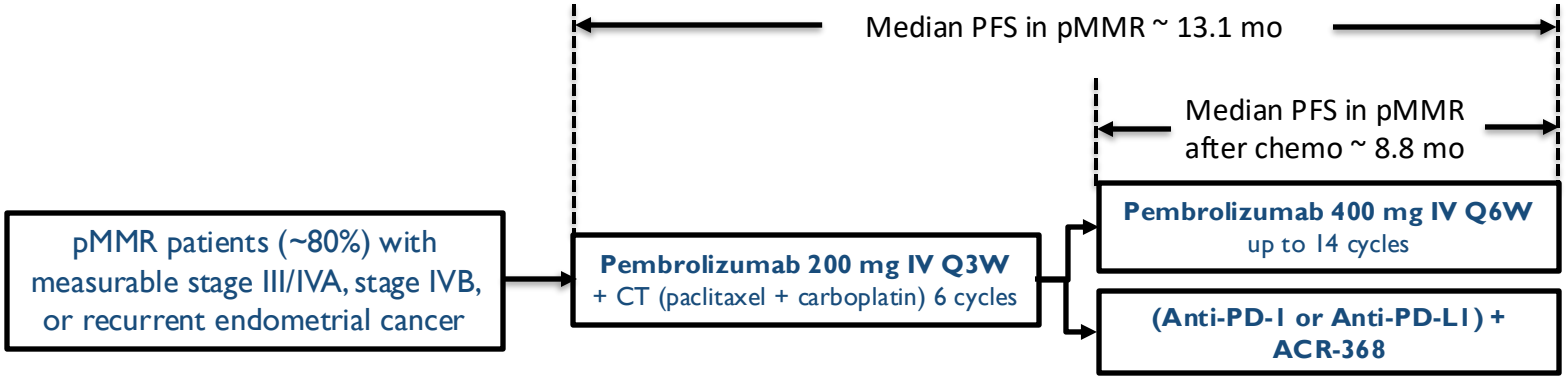
Dosing stopped in Day 34.
4/8 PRs (TV<10 mm³) showed no sign of tumor regrowth after 12 days off-treatment, suggesting 7/8 total CRs.

ACR-368 (10 mg/kg) + anti-PD-L1



Dosing stopped in Day 34.
3/8 CRs showed no sign of tumor regrowth after 12 days off-treatment.

CONFIRMATORY TRIAL OPTION: FIRST LINE LABEL EXPANSION OPPORTUNITY WITH ACR-368 AS SWITCH MAINTENANCE



Large addressable total annual market (TAM) opportunity (US only)

- OncoSignature+ patients: ~(30,000 EC x 80% pMMR x 30% BM+ x >10 months mPFS)
- All-comer patients: ~(30,000 EC x 80% pMMR x >10 months mPFS)

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

- Myelodysplastic Syndrome (MDS) and Myeloproliferative Neoplasms (MPN):
  - Prevalent (~50%) mutations in splicing factor (SF) genes (SF3B1, U2AF1, SRSF2) resulting in hyperactivated CHK [1,2]
  - Preclinical murine transplant studies of SF3B1-mutated human HSCs show potent ACR-368 single agent activity
  - High unmet need and prevalence (>400K in the US), decades of blood transfusion dependency, fatal myelofibrosis

- Squamous Cell Cancer (SCC):
  - ACR-368 has also shown promising clinical activity in HPV+ SCC and sarcomas[3]
  - HPV+ SCC increasing incidence (~50K+/y/US); ~75% oropharyngeal H&N, ~20% of esophageal, ~90% of cervical, and 95% of anal cancers[4]
  - SCCHN: Dr. Chung, Moffitt Cancer Center has begun an IIT (ACR-368 + ULDG post anti-PD-1

RECRUITING

A Phase II Study of ACR-368 and Low Dose Gemcitabine in R/M HNSCC

ClinicalTrials.gov ID NCT06597565

Sponsor H. Lee Moffitt Cancer Center and Research Institute

Information provided by H. Lee Moffitt Cancer Center and Research Institute (Responsible Party)

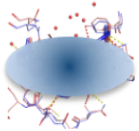
Last Update Posted 2024-09-19

[1]Sarchi et al, Blood Cancer Discovery 2024; [2]Malcovati et al, NEJM 2011
[3]Hong et al, CCR 2018, Slotkin et al, ASCO Annual Meeting 2022; [4]CDC 2023; ICO/IARC Information Centre on HPV and Cancer 2023; Gribb et al, Dela J Public Health 2023, NCI 2023

INTERNAL PIPELINE: AP3-BASED DRUG DISCOVERY

Program 1: ACR-2316, a novel dual WEE1/PKMYT1 inhibitor

- >40 high resolution co-crystals (1.5-3.1 Å) and novel WEE1- and PKMYT1-selective structural series and lead candidates

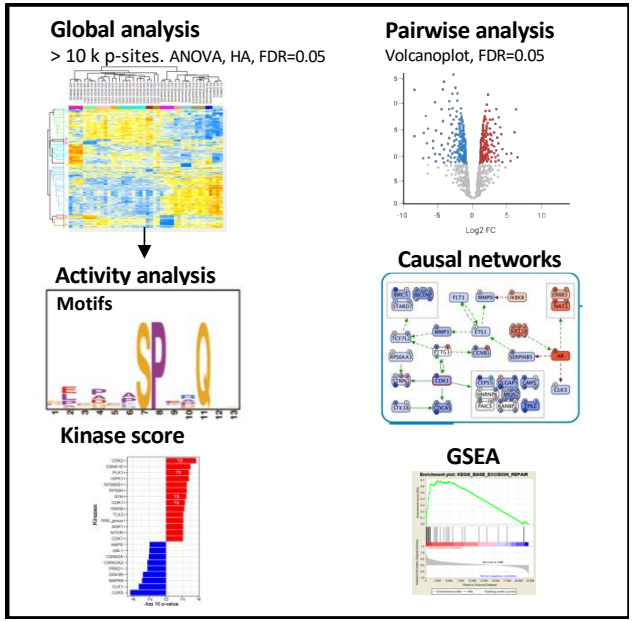


- ACR-2316 a novel, potent, selective dual inhibitor
- Designed by AP3 to overcome WEE1 and PKMYT1 single inhibitor resistance
- IND cleared and clinical sites activated Q3 2024
- First in human dosing started October 2024

Program 2: Cell cycle inhibitor with an undisclosed target

- Anticipated development candidate 2025

High throughput AP3 profiling



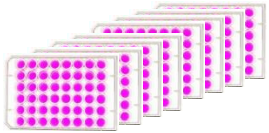
AP3 used for biologically relevant selectivity profiling

ACR-2316, A NOVEL WEE1/PKMYT1 INHIBITOR UNIQUELY ENABLED BY AP3

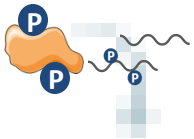
- *Optimized for superior single agent activity and therapeutic index*
- *Streamlined development: Internally discovered and advanced in 15 months from initial lead to first patient dosed in phase 1*

AP3 MASS SPECTROMETRY: STREAMLINED WORKFLOW WITH MACHINE LEARNING-AMENABLE, STRUCTURED ANALYSES

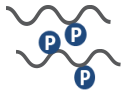
Drug treatment



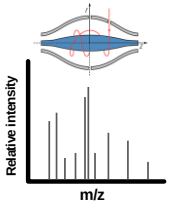
Proteolysis
P-peptide enrichment



Peptide clean up



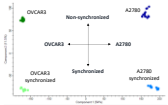
Ultra high resolution
P-proteomic profiling



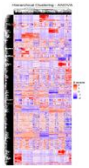
Direct DIA analysis

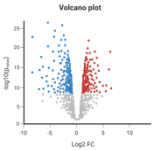
High resolution and throughput MS-based P-proteomics

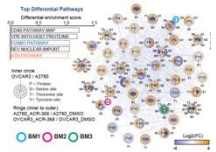
Quantitative mapping (>130,000 phospho-sites covering >9,000 proteins)



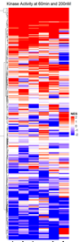
Drug-regulated phospho-sites and biological process enrichment

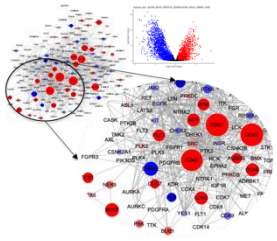


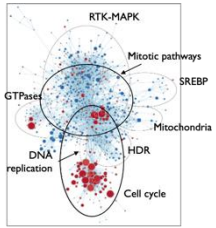




Drug-regulated pathway activity mapping and reconstitution







Proprietary pipe for automated AP3 analyses with actionable results

Week 0

Turn-around <2 weeks

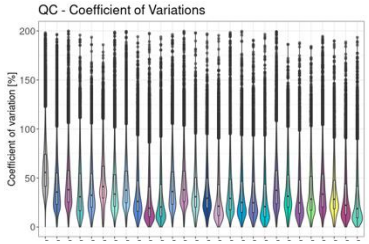
Week2

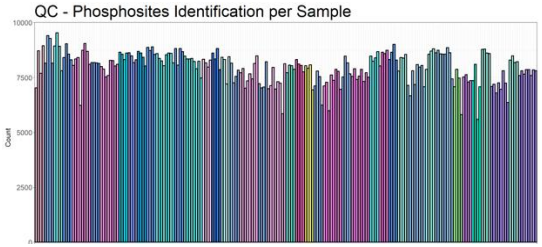
AP3: TIGHT, HIGH-RESOLUTION DATA WITH DEEP COVERAGE

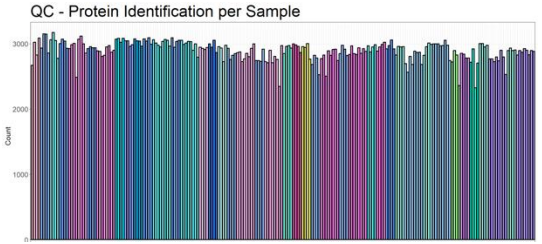
117,200 p-sites

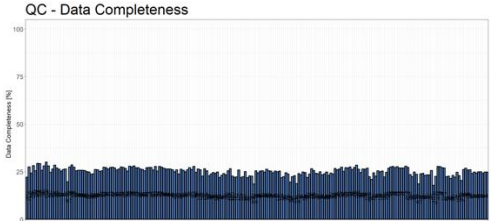
43,000 p-sites

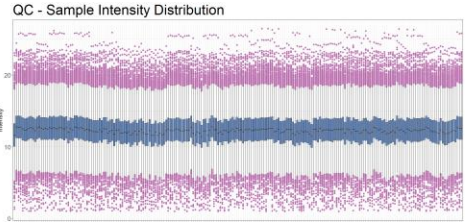
QC MS Data → Data Clean Up → QC Processed Data → Volcano Plots → Hierarchical Clustering → Consensus Sequence Motif → Kinase Inference → Pathway Enrichment → Functional Annotation → Network Mapping → Biomarkers

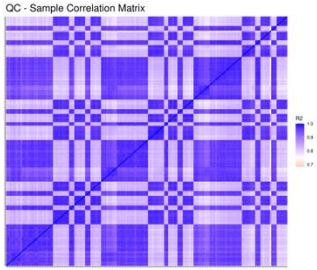










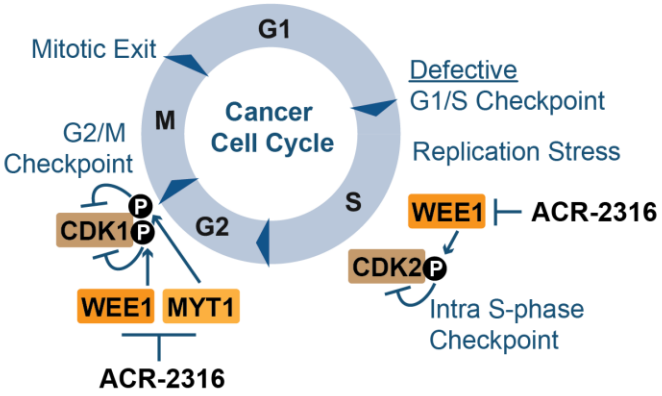


- ✓ Acrivon proprietary compound data (>150 million data points per experiment)
- ✓ Several hundred samples (quadruplicates) in each experiment; >100 compounds profiled
- ✓ Miniaturized, high throughput, scalable: <2 week turn-around, automated AI computational analyses in 1 day

Actionable AP3 results: Resistance mechanisms, rational combinations, indication finding, response prediction

INHIBITORS OF EITHER WEE1 OR PKMYT1 HAVE SHOWN LIMITED SINGLE AGENT ACTIVITY AND NARROW THERAPEUTIC INDEX

- 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
- WEE1 inhibition propagates genomic instability by premature DNA replication and cell cycle progression
- PKMYT1 inhibition results in premature mitotic entry



- Several WEE1 inhibitors and a PKMYT1 inhibitor have demonstrated anti-tumor activity in clinical trials across solid tumor types
- Current clinical agents challenged by lack of predictive biomarkers and narrow therapeutic index, limiting safety and efficacy

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

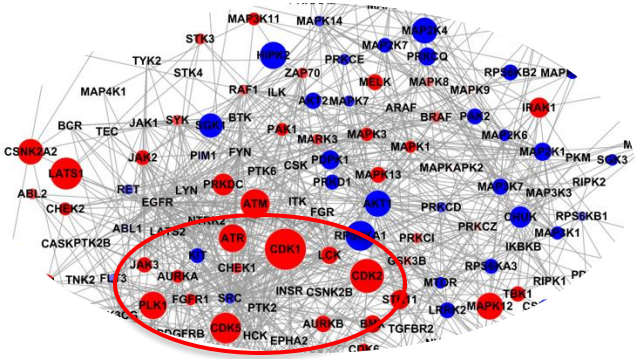
Program goals (superior therapeutic index):

- **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

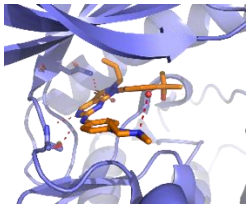
ACR-2316: Rationally designed WEE1/PKMYT1 inhibitor

- ✓ 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

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 IS A POTENTIALLY BEST- AND FIRST-IN-CLASS AGENT 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 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 safety profile		▪ Potent tumor cell killing, short elim. $T_{1/2}$, and high selectivity at weekly on-off schedule results in only transient, reversible, mechanism-based AEs
4 Streamlined clinical development		▪ Broad preclinical therapeutic index and anti-tumor activity across all dosing regimens ▪ AP3-based identification of PD biomarkers and prioritization of promising indications

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

ACR-2316 SHOWS SUPERIOR PRECLINICAL POTENCY VS BENCHMARK WEE1/PKMYT1 INHIBITORS[1]

		ACR-2316[2]	SGR-3515[3]	Azenosertib[2]	Lunresertib[2]	Adavosertib[2]	Debio0123[2]
Binding (nM)	WEE1	1	0.06	2 vs 1.2	31 vs ND	1	1
	PKMYT1	27	15	337 vs 300	10 vs 0.02	155	>2000
Cellular TE (nM)	WEE1	2	65	16 vs 280	> 5000 vs 4200	19	109
	PKMYT1	145	230	> 5000 vs 4600	11 vs 54	4000	>5000
Viability IC50 (nM)	A427 (Mean)	30	80	289 vs 200	352 vs 280	180	541
	All Lines (Median)	50 (n=27)	92 (n=139)	340 (n=27) vs 319 (n=120)	281 vs 782 (n=91)	249 (n=27)	680 (n=23)
	All Lines (Range)	10-286 (n=27)	15-716 (n=139)	53 to > 1000 (vs 10-7913)	33 to > 1000 (vs 10-10000)	52 to 920 (n=27)	184 to >1000 (n=23)

Black text = Acrivon Data; Grey text = Schrodinger Data

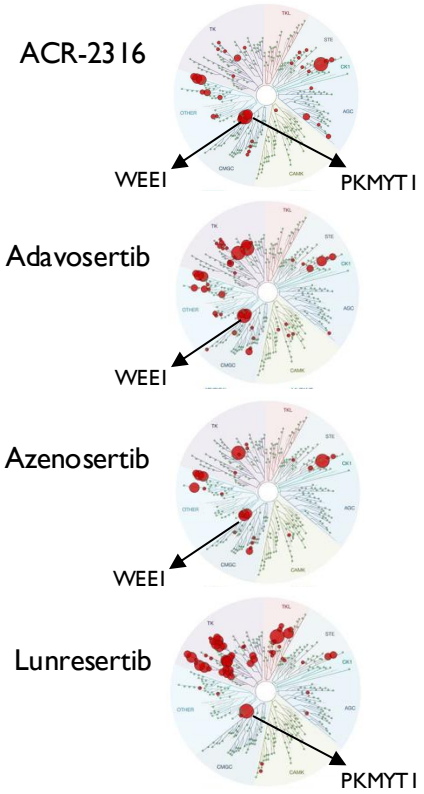
[1]Head-to-head preclinical studies against benchmarks with clinical data

[2]Binding and cellular target engagement data for ACR-2316 vs. azenosertib, lunresertib, adavosertib and Debio 0123 presented at AACR 2024

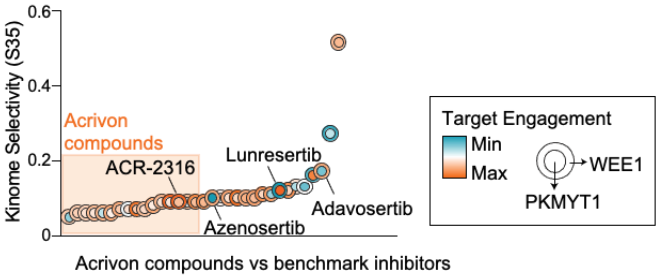
[3]SGR-3515 preclinical data presented at ENA-2024

DUAL WEE1/PKMYT1 INHIBITOR ACR-2316 DEMONSTRATES STRONG POTENCY AND SELECTIVITY

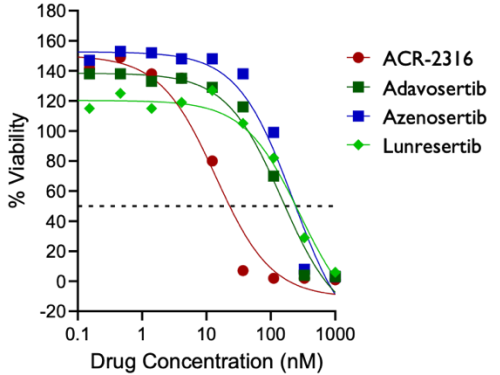
KinomeScan (468 kinases @ 1μM)



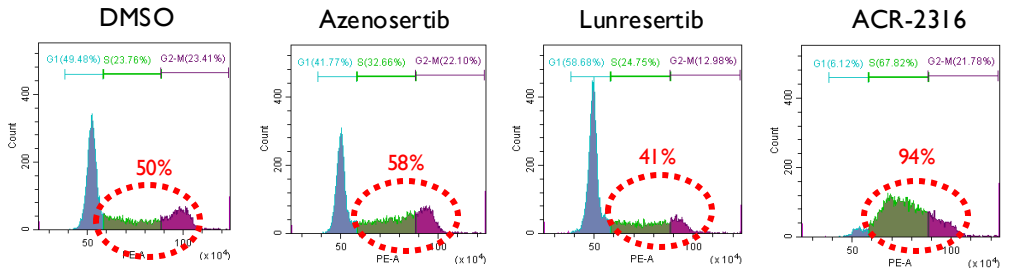
ACR-2316 is highly selective (KinomeScan)



ACR-2316 potently inhibits cancer cell viability

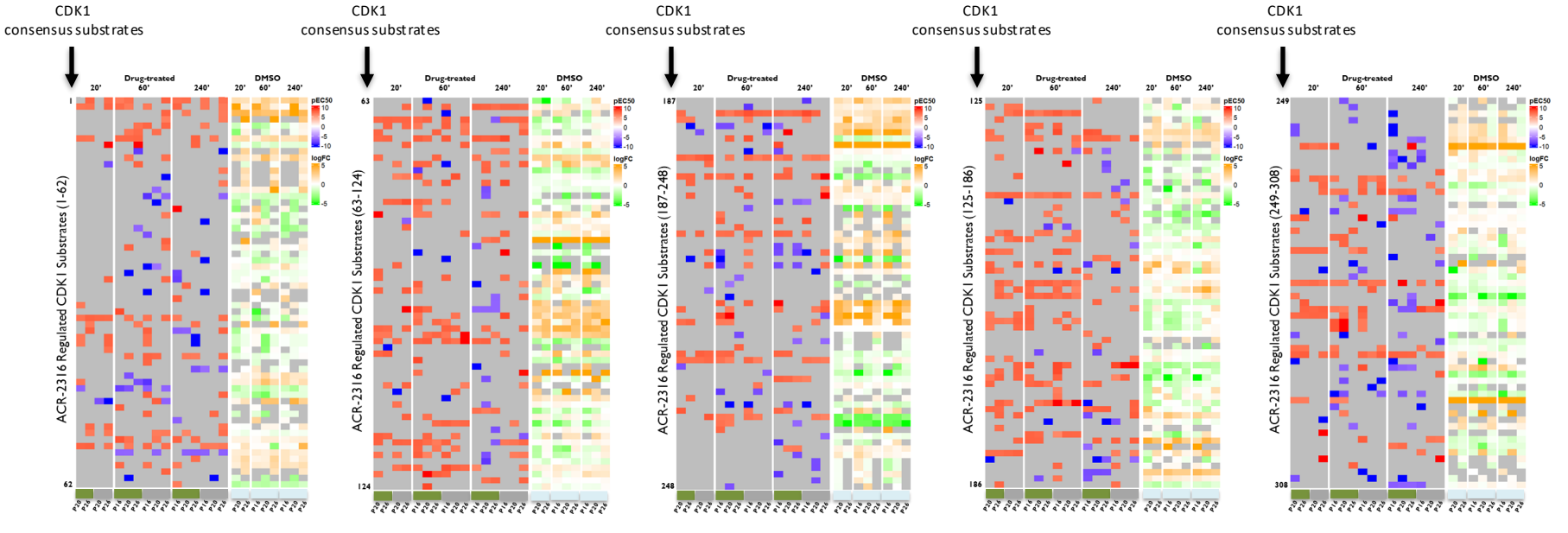


ACR-2316 exerts potent cell cycle effects with pronounced S-G2/M accumulation



100 nM, 24 hour

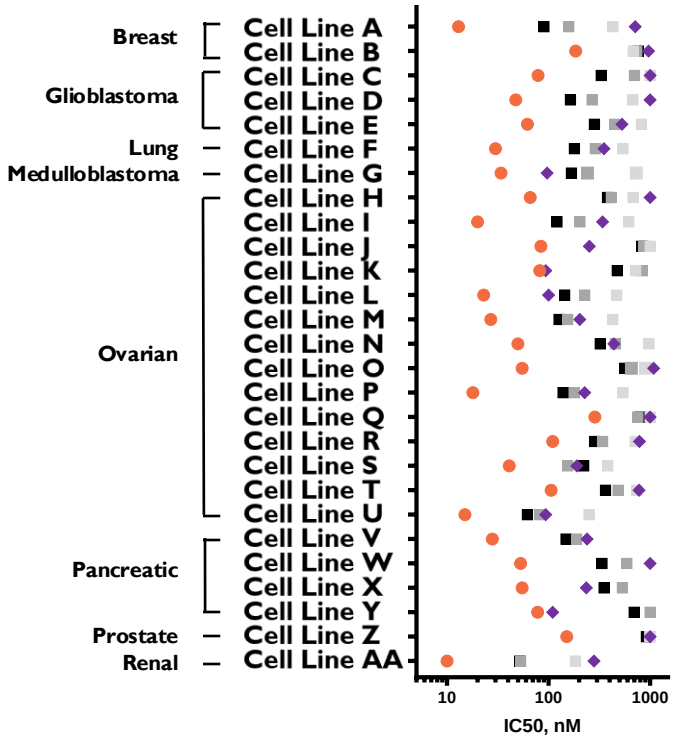
ACR-2316 RESULTS IN STRONG ACTIVATION OF CDK1 ACROSS CELL LINES



- Unbiased quantitation of ACR-2316-regulated CDK1 substrate p-sites (308) in intact cells based on CDK1 consensus recognition motif (Acrivon proprietary hybrid database approach) across multiple experiments
- Actionable insight into drivers of mitotic catastrophe and on-target CDK1-driven pathways

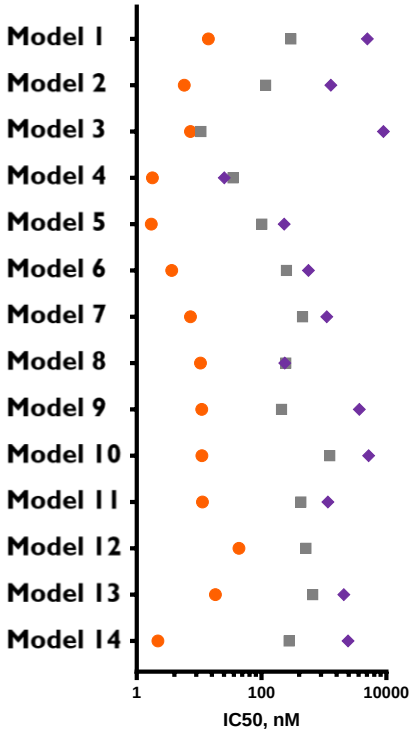
ACR-2316 IS HIGHLY POTENT ACROSS HUMAN TUMOR CELL LINES AND PATIENT-DERIVED *EX VIVO* TUMOR MODELS

Human tumor cell lines (not genetically selected)

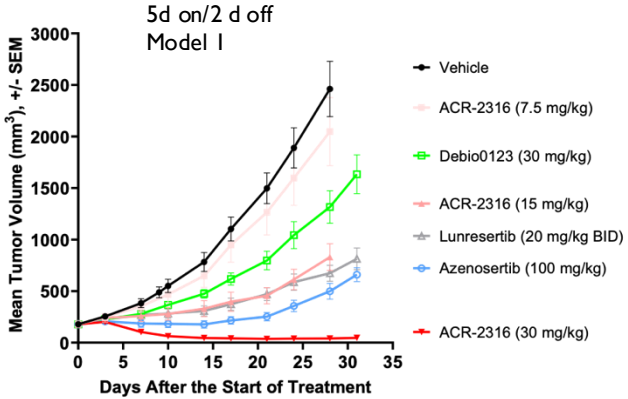


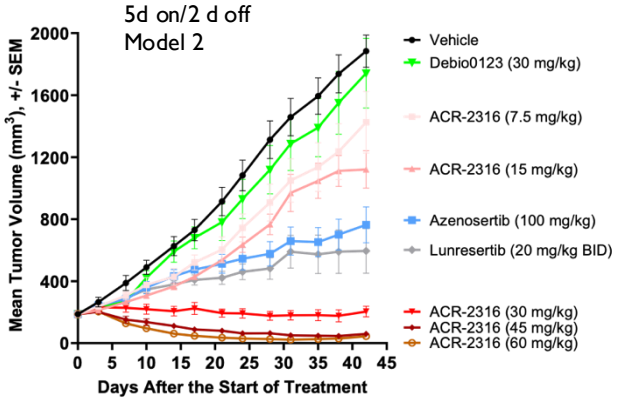
ACR-2316
Adavosertib
Azenosertib
Debio 0123
WEE1i
Lunresertib
PKMYT1i

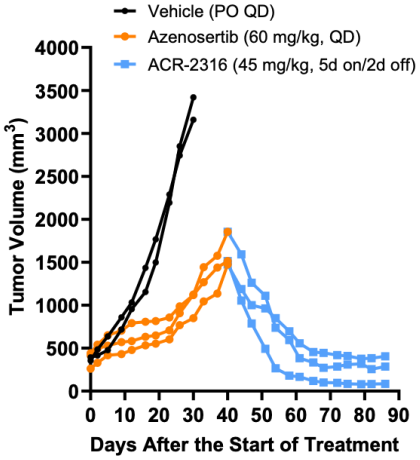
Patient-derived *ex vivo* ovarian tumor models

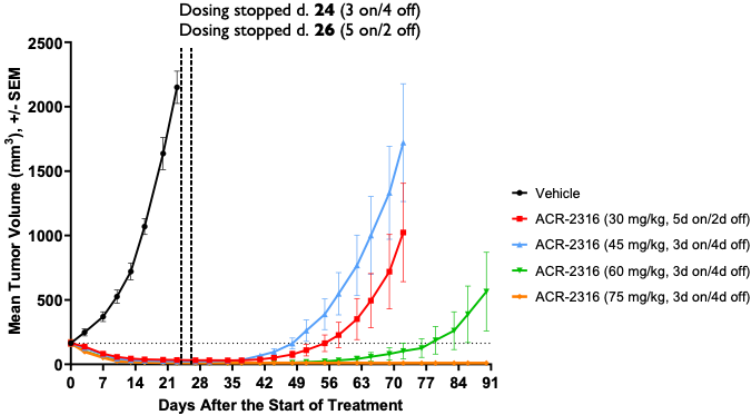


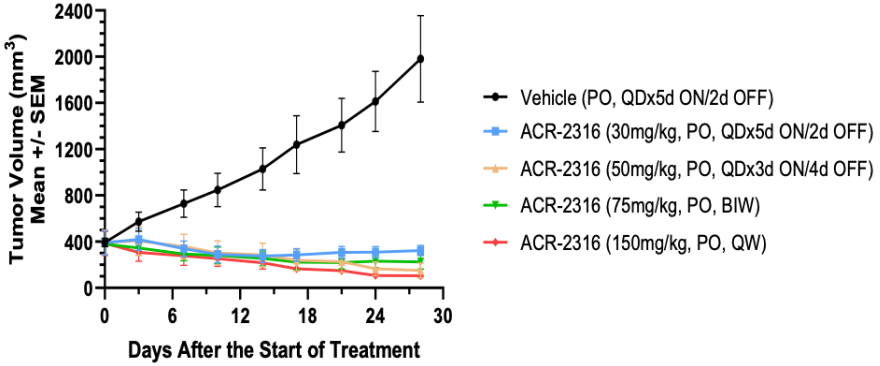
ACR-2316 INDUCES COMPLETE TUMOR REGRESSION ACROSS MODELS AND DOSING REGIMENS











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

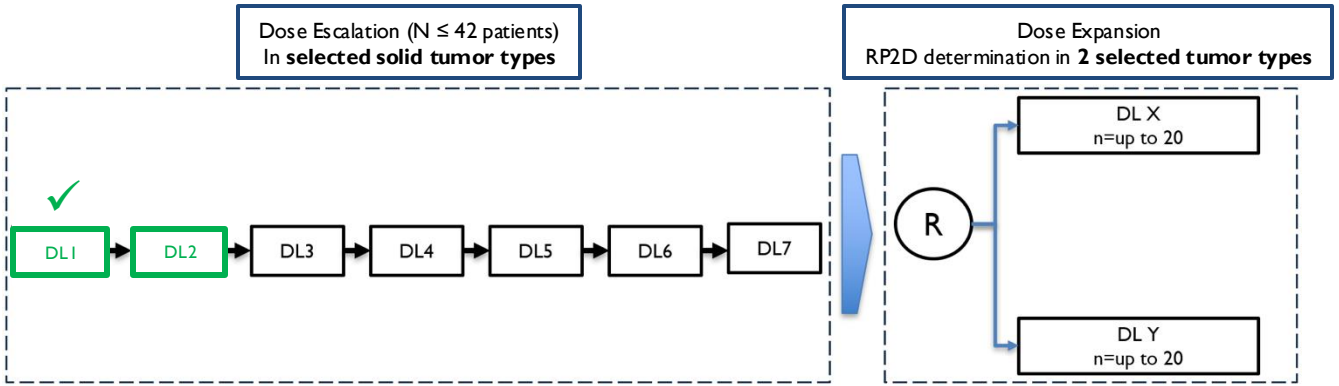
Rat and dog MTD, DRF, and GLP tox studies:

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

The broad therapeutic index observed across all our preclinical studies conducted with the same dosing regimen used in our ongoing Phase 1 trial is consistent with the predicted target human exposure required for anti-tumor activity and anticipated reversibility of mechanism-based AEs

ACR-2316 PHASE 1 PATIENT ENROLLMENT AND DOSING ONGOING

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

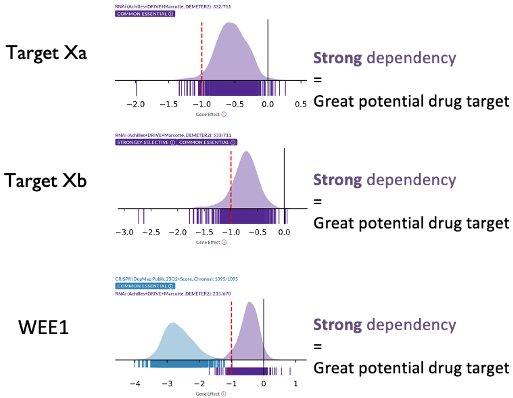


Aiming for streamlined clinical development:

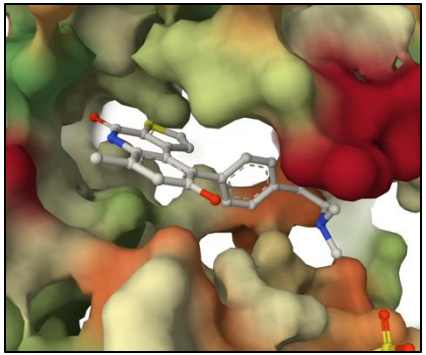
- ACR-2316 advanced in 15 months from initial lead into Phase 1 uniquely enabled by AP3
- AP3-based indication finding has identified highly commercially attractive indications
- Dose optimization guided by drug target engagement aligned with Project Optimus

PROGRAM 2: CELL CYCLE REGULATOR (UNDISCLOSED TARGET)

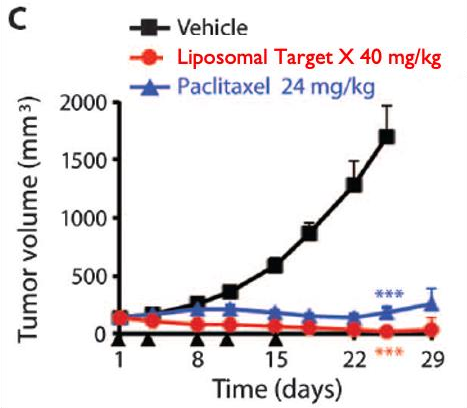
- Target X – an exciting cancer drug target, no/minimal competitor programs, perfectly suited for AP3 platform
- DepMap data suggest suggest target X is an essential gene for cancer cell viability
- Strong mechanistic target rationale for role in oncogenesis
- Highly selective tool compound shows strong anti-tumor efficacy in rodent models
- Tool compound AP3 profiling supports selectivity
- New preclinical program leveraging co-crystallography and AP3 infrastructure successfully built for ACR-2316



Genetic dependency analysis across CCLE (n > 700)



Tool compound is a selective target X inhibitor
(originally believed to be inhibitor for another target)



Development candidate 2025

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

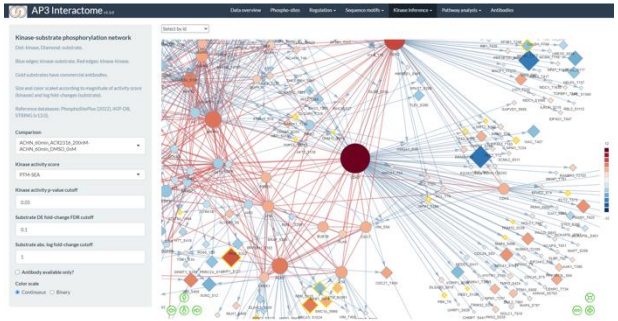
Consensus Sequence Motif

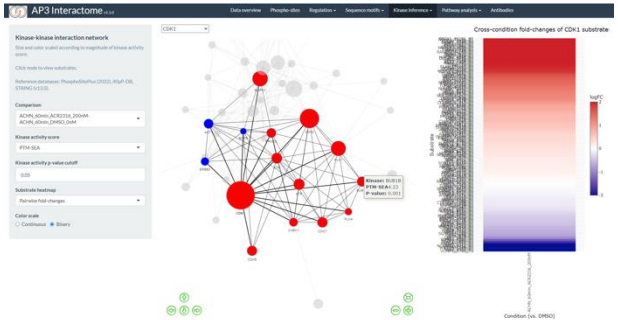
Pathway Enrichment

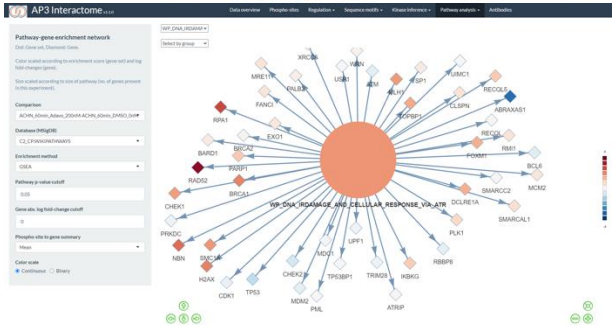
Kinase Inference

Network Mapping

Biomarkers



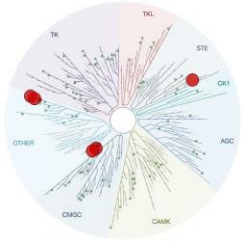




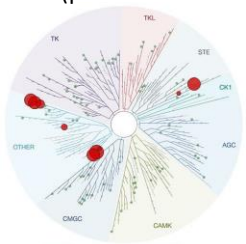
AP3 REVEALS DRUG-REGULATED KINASE ACTIVITY IN INTACT CELLS NOT DETECTABLE BY STANDARD METHODS

KinomeScan @ 1μM

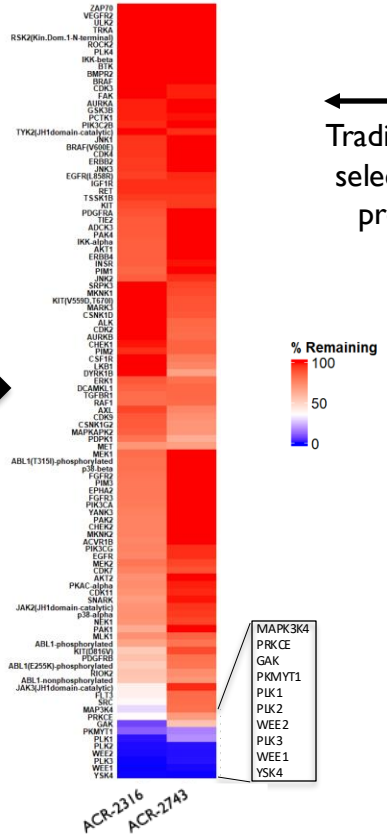
ACR-2316



ACR-2743 (previous lead candidate)



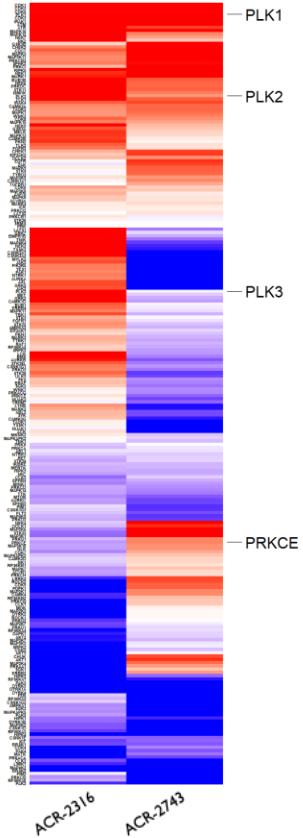
Time : 60 minutes
Dose : 20 nM

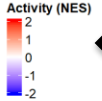


Traditional selectivity profiling

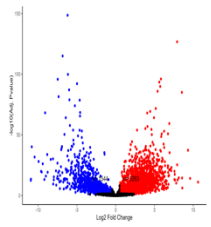
AP3-based pathway profiling

Drug-regulated kinase activity* in intact cells

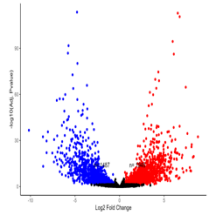




ACR-2316



ACR-2743

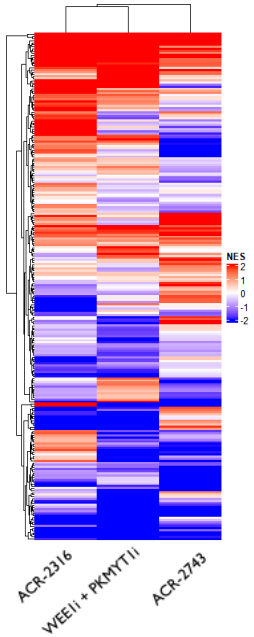


*Kinase activity based on substrate motif analysis using a proprietary PTM-SEA hybrid method

OPTIMIZED DUAL INHIBITORS SHOW DESIRABLE PATHWAY EFFECTS

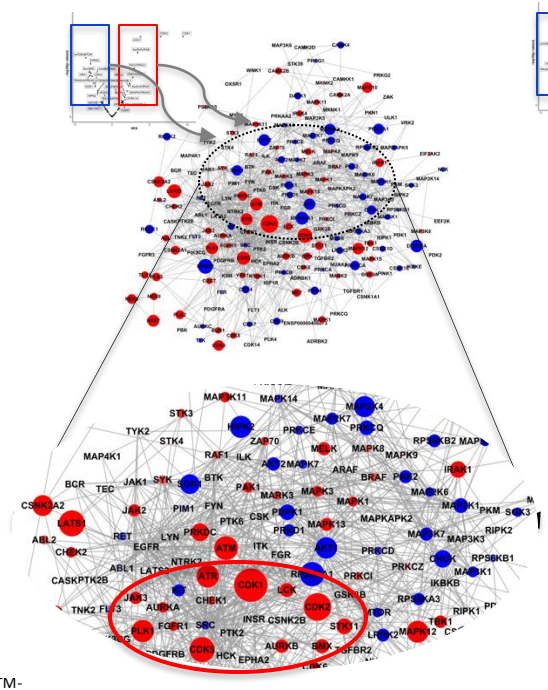
Optimized dual WEE1 and PKMYT1 inhibitors affect cell cycle and canonical MAPK pathways in desirable manner

Substrate motif-inferred kinase activities

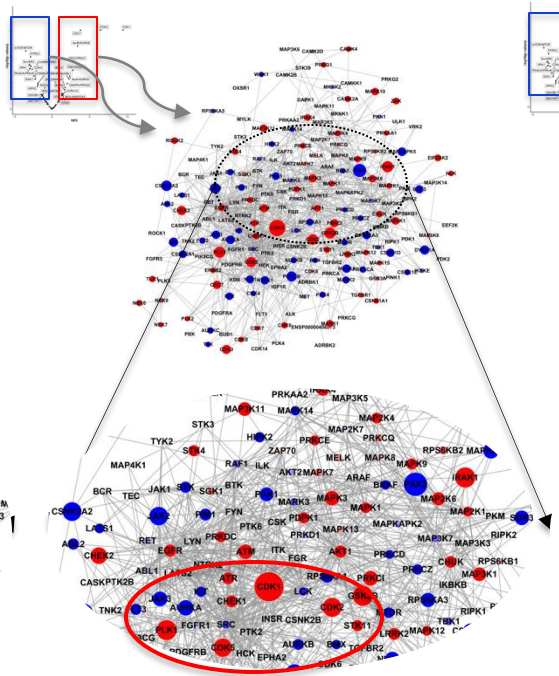


Kinase activity based on proprietary PTM-SEA-based hybrid workflow and analyses

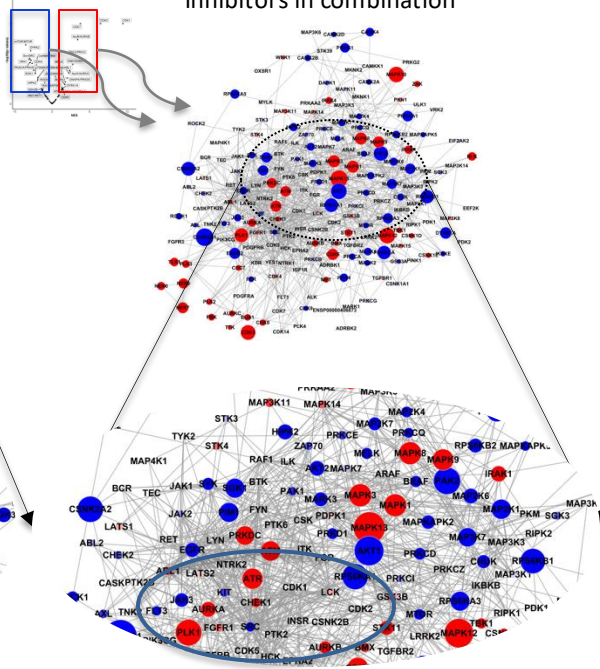
ACR-2316

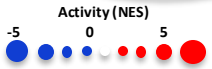


ACR-2743



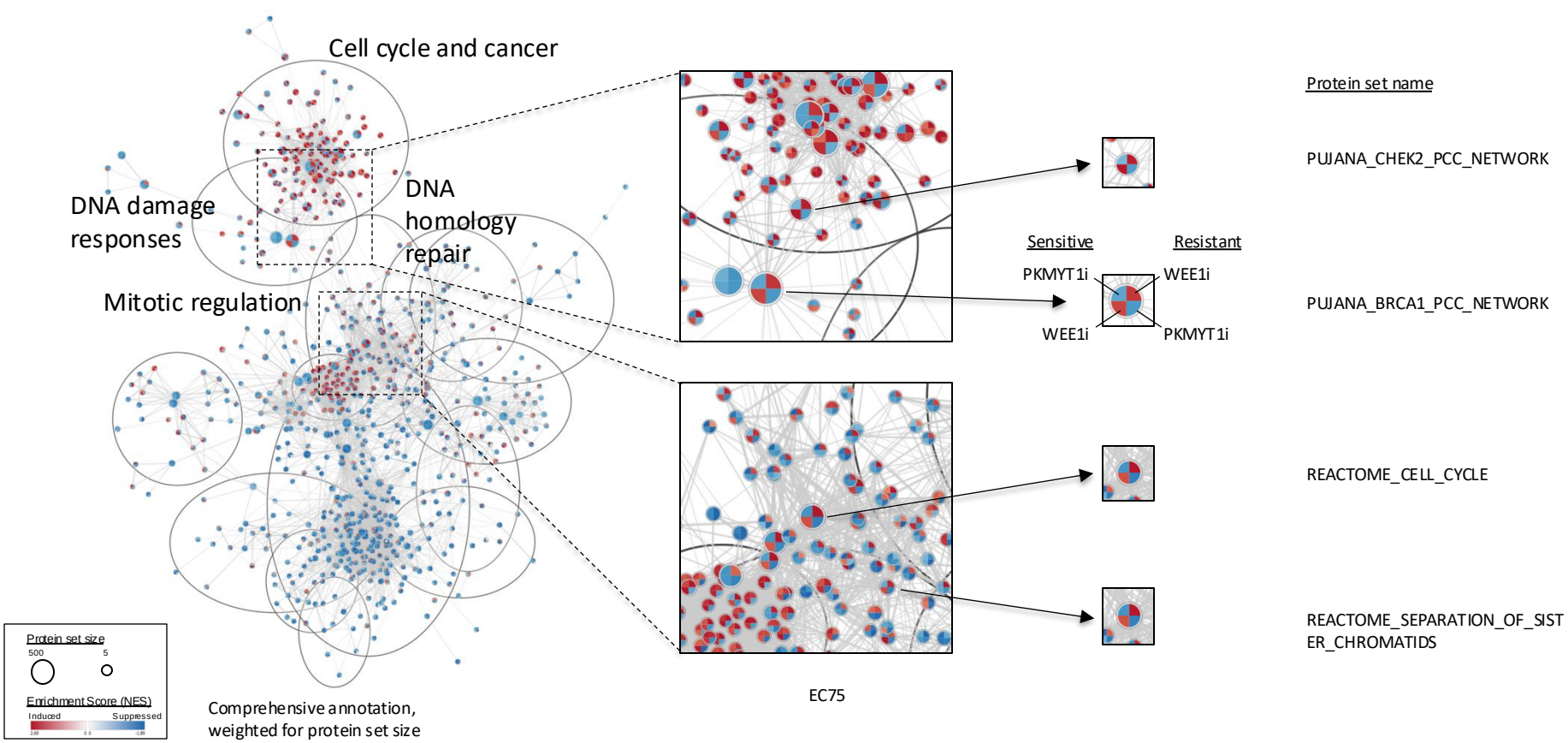
Benchmark* WEE1 + PKMYT1 Inhibitors in combination



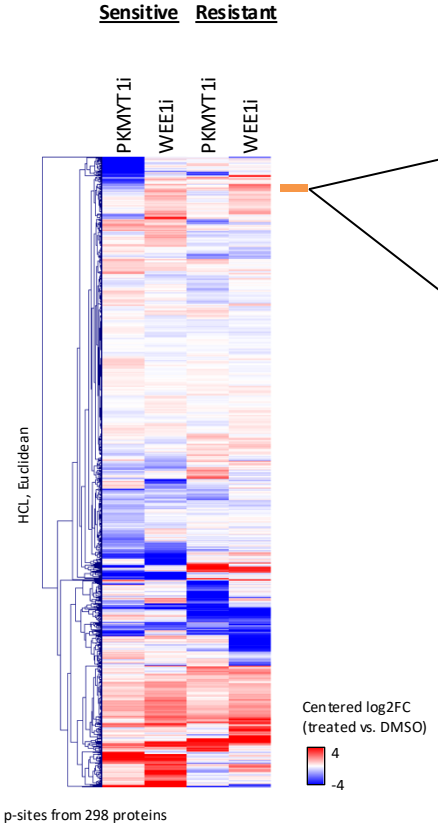


*Clinical-stage selective WEE1 and PKMYT1 inhibitors

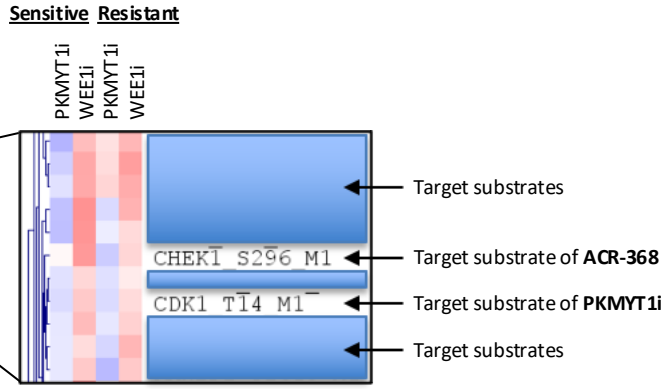
AP3-DERIVED DUAL POTENCY OPTIMIZATION TO OVERCOME WEE1 INHIBITOR RESISTANCE: RECIPROCAL QUENCHING



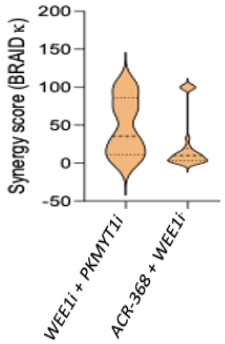
AP3 RECIPROCAL QUENCHING REVEALS OPTIMAL TARGET POTENCY PROFILE FOR DUAL WEE1/PKMYT1 INHIBITOR



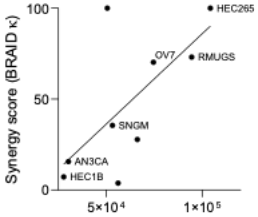
1043 p-sites from 298 proteins



Optimal potency ratio results in significant synergy



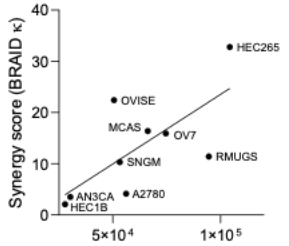
WEE1i and PKMYT1i dual inhibition synergy



WEE1 inhibitor sensitivity (Mean AUC)

Pearson r = 0.68
p value = 0.0459

WEE1i and ACR-368



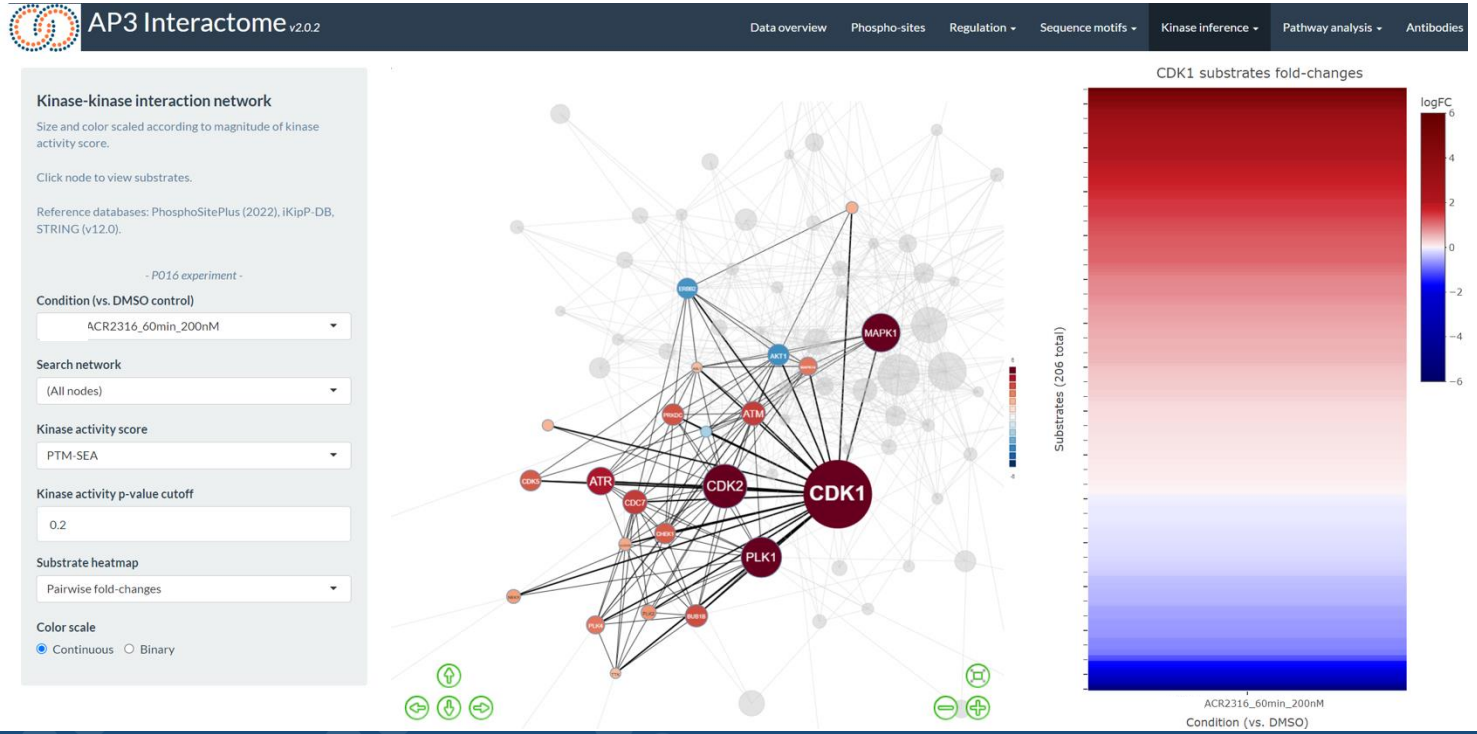
WEE1 inhibitor sensitivity (Mean AUC)

Pearson r = 0.71
p value = 0.0324

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



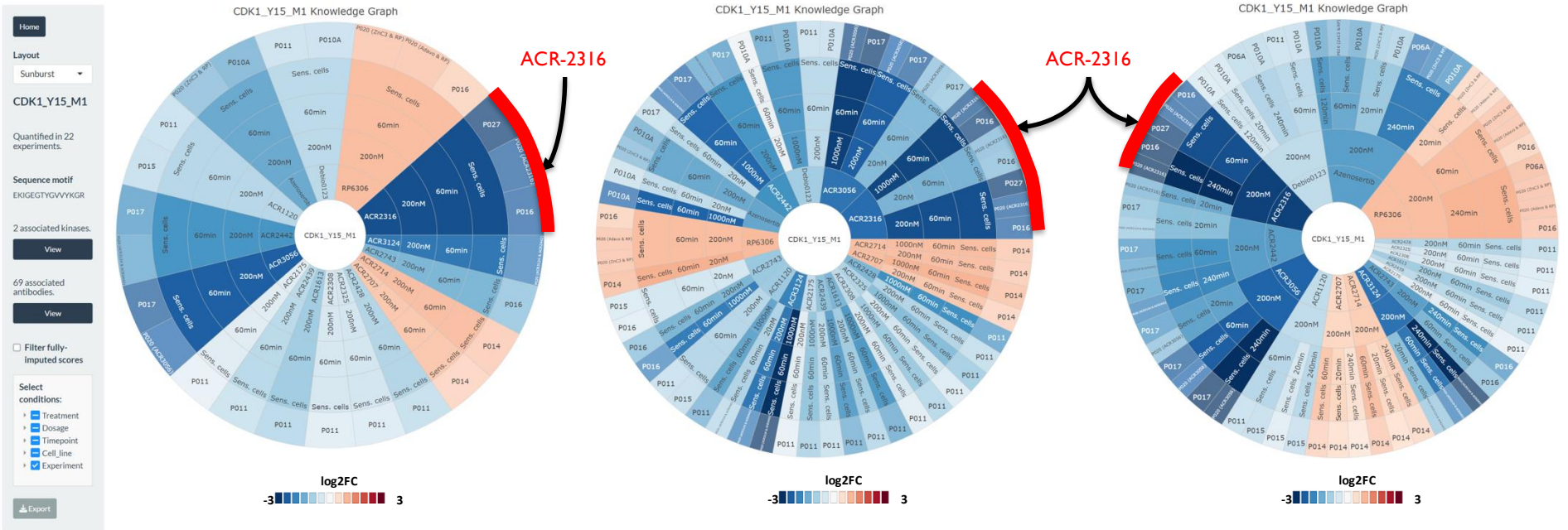
ROBUST POTENT INHIBITION OF CDK1 CONSENSUS SUBSTRATE Y15 BY ACR-2316

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

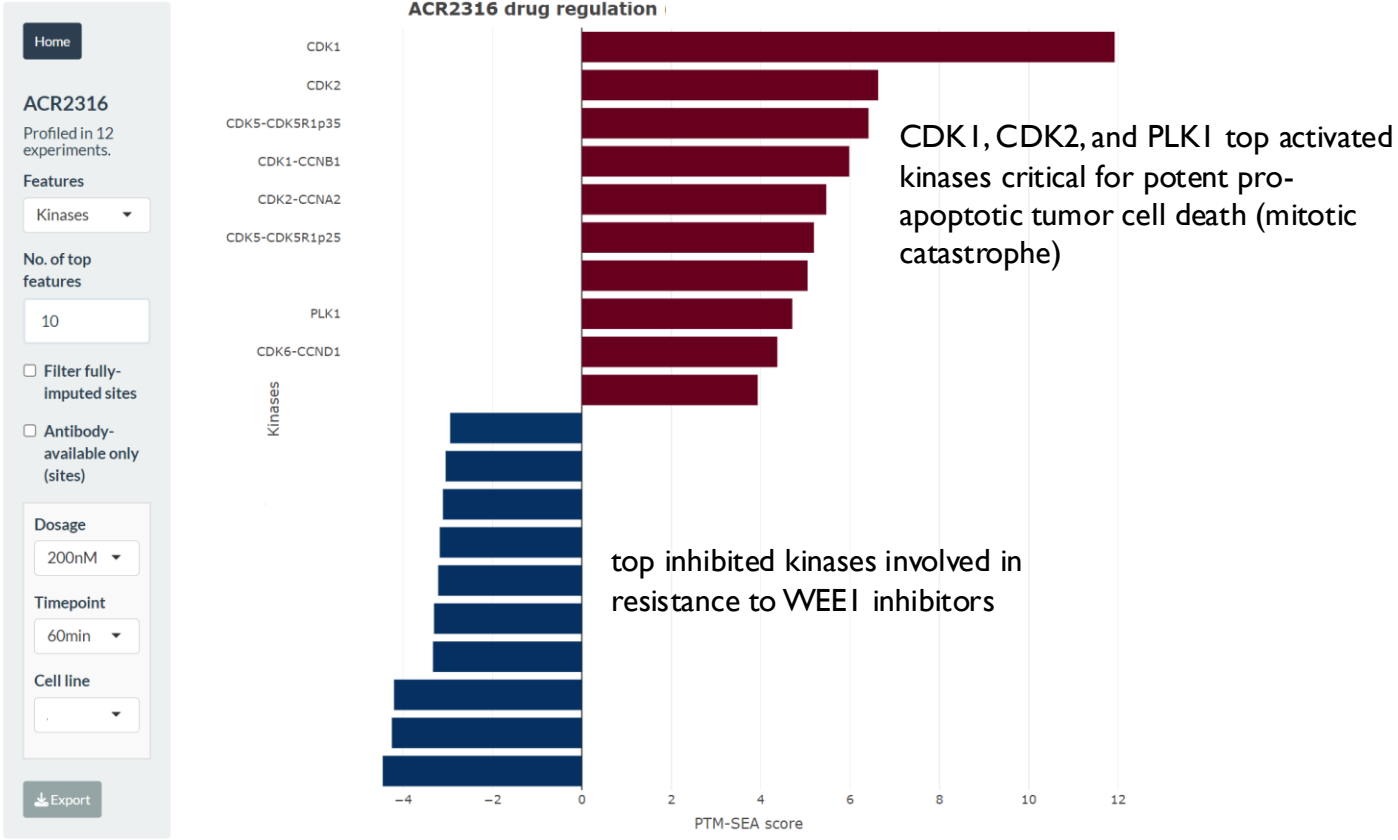
Comparison
@60min and 200nM in ACHN

Dose-dependent comparison
@ 60min in ACHN

Time-dependent comparison
@ 200nM in ACHN



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



DATA DRIVEN EXECUTION AND VALUE CREATION

Recent Accomplishments (Last 12 Months)

- ✓ Positive ACR-368 data (ESMO 2024) in registrational intent endometrial cancer trial (ORR >60%; OncoSignature validation p = 0.009)
- ✓ Positive initial ACR-368 clinical data in ovarian and endometrial cancer patients (ORR = 50%) in Q2 2024
- ✓ IND clearance for ACR-2316 (Q3 2024) and first patient dosed in Q4 2024 (2 quarters ahead of schedule) with initial lead to Phase 1 initiation achieved in 15 months, uniquely enabled by AP3
- ✓ Corporate R&D Events (Q2 and Q3 2024) presenting positive clinical and preclinical pipeline data and AI/ML-driven AP3 Interactome
- ✓ Presented preclinical data on ACR-2316 and ACR-368 resistance mechanisms uncovered by AP3 (AACR Q2 2024)
- ✓ Completed Phase 1b and initiated Phase 2 study of ACR-368 + LDG for OncoSignature-negative patients Q1 2024
- ✓ Completed oversubscribed $130M PIPE financing at premium Q2 2024

Anticipated Next Milestones (2025)

Phase 2 program updates for ACR-368 1H 2025

Initial clinical data for ACR-2316 Phase 1 trial 2H 2025

Development candidate nomination for novel cell cycle program with an undisclosed target 2025

Target/compound validation and indication finding for new program in autoimmune/inflammatory diseases leveraging AP3

FINANCIAL HIGHLIGHTS

Cash and marketable securities

$202.8M

Balance sheet 30-Sept-2024

Projected runway into

H2'26

Current operating plan, assuming no additional financing

Fully Diluted Shares Outstanding

43.7M

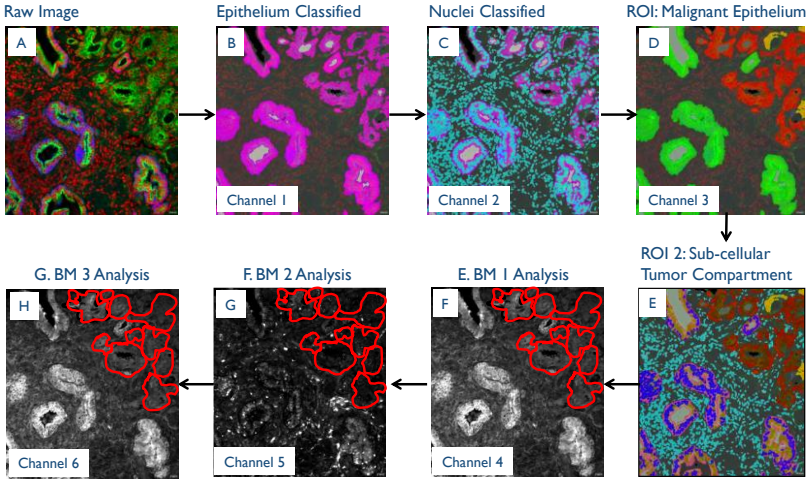
Including shares, pre-funded warrants and equity grants outstanding 30-Sept-2024

Note: Unaudited.

APPENDIX

TEAM HAS PIONEERED OUTCOME-PREDICTIVE QUANTITATIVE PROTEOMIC MULTIPLEX IN SITU TEST

Prostate cancer 8-marker biopsy test developed and launched by Founding team



- ProMark®: Marketed, automated *in situ* proteomic test for human outcome prediction included under NCCN guidelines
- Founding team: Has pioneered p-proteomics and quantitative multiplex imaging including double-blinded clinical validation*

Ideal test	Protein multiplex *in situ* test	Current CDx tests
Quantitative and automated	✓	(✓)
Validated Abs and reagents	✓	(✓)
Drug target and pathway activation context	✓	
Biomarkers measured in relevant region on tumor biopsy	✓	
Imaging algorithm (tissue pattern)	✓	
Addresses tumor heterogeneity	✓	
Double-blinded, prospective validation	✓	(✓)

*Blume-Jensen et al: Development and clinical validation of an *in situ* biopsy-based multimarker assay for risk stratification in prostate cancer. Clinical Cancer Research (2015)

PROOF-OF-CONCEPT FOR PROTEIN BIOMARKER SIGNATURE: MARKETED, OUTCOME-PREDICTIVE MULTIPLEX CANCER TEST

Biology of Human Tumors

Clinical Cancer Research

(2015)

Development and Clinical Validation of an *In Situ* Biopsy-Based Multimarker Assay for Risk Stratification in Prostate Cancer

Peter Blume-Jensen[1], David M. Berman[2], David L. Rimm[3], Michail Shipitsin[1], Mathew Putzi[4], Thomas P. Nifong[1], Clayton Small[1], Sibgat Choudhury[1], Teresa Capela[1], Louis Coupal[5], Christina Ernst[1], Aeron Hurley[1], Alex Kaprelyants[1], Hua Chang[1], Eldar Giladi[1], Julie Nardone[1], James Dunyak[1], Massimo Loda[6], Eric A. Klein[7], Cristina Magi-Galluzzi[8], Mathieu Latour[9], Jonathan I. Epstein[10], Philip Kantoff[6], and Fred Saad[9]

- Third-party blinded clinical validation, bioinformatic analysis (U. Montreal)
- Validation of locked ProMark™ test on single institution biopsy cases (N=274)
- Secondary validation on multi-center biopsy cohort (N=359) for clinical use indication
- Marketed test included under NCCN Guidelines and Medicare coverage

PIONEERING PHOSPHO-PROTEOMICS STUDY IDENTIFIES NOVEL PI3K PATHWAY INHIBITOR BIOMARKERS

Science Translational Medicine
AAAS

Sci Transl Med
2: 1-14 (2010)

RESEARCH ARTICLE

CANCER DRUG DEVELOPMENT

Pathway-Based Identification of Biomarkers for Targeted Therapeutics: Personalized Oncology with PI3K Pathway Inhibitors

Jannik N. Andersen,[1]* Sriram Sathyanarayanan,[1]* Alessandra Di Bacco,[1] An Chi,[1] Theresa Zhang,[1] Albert H. Chen,[1] Brian Dolinski,[1] Manfred Kraus,[1] Brian Roberts,[1] William Arthur,[2] Rich A. Klinghoffer,[1†] Diana Gargano,[1‡] Lixia Li,[1] Igor Feldman,[1] Bethany Lynch,[1] John Rush,[3] Ronald C. Hendrickson,[4§] Peter Blume-Jensen,[1§‖] Cloud P. Paweletz[1]

Editorial Highlights:

VOLUME 28 NUMBER 10 OCTOBER 2010 NATURE BIOTECHNOLOGY

Tracing cancer networks with phosphoproteomics

David B Solit & Ingo K Mellinghoff

A mass-spectrometry approach for identifying downstream events in cancer signaling pathways may help to tailor therapies to individual patients.

Science Translational Medicine
AAAS

TOWARD CUSTOMIZING TUMOR TREATMENT

Just as our view of Earth has become increasingly global, cells are now seen as complex networks of interacting and intersecting signaling pathways rather than a collection of regulated genes.

Nature Reviews Cancer | AOP, published online 19 August 2010; doi:10.1038/nrc2922

A discovery strategy for novel cancer biomarkers

OLSEN LAB-EXAMPLES OF DEEP PROTEOMICS DRUG PROFILING

Science Signaling (2018)

ALK-i : LDK378, TAE684, crizotinib, lorlatinib.

SCIENCE SIGNALING | RESEARCH RESOURCE

CANCER

Integrated proximal proteomics reveals IRS2 as a determinant of cell survival in ALK-driven neuroblastoma

Kristina B. Emdal[1,2†], Anna-Kathrine Pedersen[1†], Dorte B. Bekker-Jensen[1], Alicia Lundby[1,3], Shana Claeys[4], Katleen De Preter[4], Frank Speleman[4], Chiara Francavilla[1,5‡‖], Jesper V. Olsen[1‡‖]

Cell Reports (2018)

SHP2-i: SHP099 -allosteric inhibitor.

Large-Scale Phosphoproteomics Reveals Shp-2 Phosphatase-Dependent Regulators of Pdgf Receptor Signaling

Tanveer S. Batth,[1,4] Moreno Papetti,[1,4] Anamarija Pfeiffer,[1] Maxim A.X. Tollenaere,[2] Chiara Francavilla,[1,2,*] and Jesper V. Olsen[1,5,*]
[1]Proteomics Program, Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Science, University of Copenhagen, Blegdamsvej 3B, 2200 Copenhagen, Denmark
[2]Cellular Stress Signaling Group, Department of Cellular and Molecular Medicine, Center for Healthy Aging, University of Copenhagen, 2200 Copenhagen, Denmark
[3]School of Biological Sciences, FBMH, University of Manchester, Oxford Road, Manchester M13 9PT, UK
[4]These authors contributed equally
[5]Lead Contact
*Correspondence: chiara.francavilla@manchester.ac.uk (C.F.), jesper.olsen@cpr.ku.dk (J.V.O.)
https://doi.org/10.1016/j.celrep.2018.02.038

Cell Reports (2017)

CHK1-i: SCH900776, **ATM-i:** KU55933

Proteomics Reveals Global Regulation of Protein SUMOylation by ATM and ATR Kinases during Replication Stress

Stephanie Munk,[1,2,4] Jón Otti Sigurðsson,[1,4] Zhenyu Xiao,[3,4] Tanveer Singh Batth,[1] Giulia Francioso,[1] Louise von Stechow,[1] Andres Joaquin Lopez-Contreras,[2] Alfred Cornelis Otto Vertegaal,[3*] and Jesper Velgaard Olsen[1,5*]
[1]Proteomics Program, Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Sciences, University of Copenhagen, 2200 Copenhagen, Denmark
[2]Center for Chromosome Stability and Center for Healthy Aging, Institute for Cellular and Molecular Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, 2200 Copenhagen, Denmark
[3]Department of Molecular Cell Biology, Leiden University Medical Center, 2300 RC Leiden, the Netherlands
[4]These authors contributed equally
[5]Lead Contact
*Correspondence: a.c.o.vertegaal@lumc.nl (A.C.O.V.), jesper.olsen@cpr.ku.dk (J.V.O.)
https://doi.org/10.1016/j.celrep.2017.09.059

Cell Reports (2017)

CDK7-i: THZ-1

Phosphoproteomics of Primary Cells Reveals Druggable Kinase Signatures in Ovarian Cancer

Chiara Francavilla,[1,4,7,*] Michela Lupia,[2,6] Kalliopi Tsafou,[3,6,8] Alessandra Villa,[2,9] Katarzyna Kowalczyk,[5] Rosa Rakownikow Jersie-Christensen,[1] Giovanni Bertalot,[4] Stefano Confalonieri,[4] Søren Brunak,[3] Lars J. Jensen,[3] Ugo Cavallaro,[2,*] and Jesper V. Olsen[1,10,*]
[1]Proteomics Program, Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Sciences, University of Copenhagen, Blegdamsvej 3B, 2200 Copenhagen, Denmark
[2]Unit of Gynecological Oncology Research, Program of Gynecological Oncology, European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy
[3]Disease Systems Biology Program, Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Sciences, University of Copenhagen, Blegdamsvej 3B, 2200 Copenhagen, Denmark
[4]Program of Molecular Medicine, European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy
[5]Division of Molecular and Cellular Functions, School of Biological Sciences, Faculty of Biology, Medicine and Health, the University of Manchester, Manchester M13 9PL, UK
[6]Co-first author
[7]Present address: Division of Molecular and Cellular Functions, School of Biological Sciences, Faculty of Biology, Medicine and Health, the University of Manchester, Manchester M13 9PL, UK
[8]Present address: Department of Oncology, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC 20057, USA
[9]Present address: Philochem AG, Otelfingen, Switzerland
[10]Lead Contact
*Correspondence: chiara.francavilla@manchester.ac.uk (C.F.), ugo.cavallaro@ieo.it (U.C.), jesper.olsen@cpr.ku.dk (J.V.O.)
http://dx.doi.org/10.1016/j.celrep.2017.03.015

Cell Systems (2017)

Deepest proteome resolution of a human cell to date

An Optimized Shotgun Strategy for the Rapid Generation of Comprehensive Human Proteomes

Dorte B. Bekker-Jensen,[1,4] Christian D. Kelstrup,[1,4*] Tanveer S. Batth,[1] Sara C. Larsen,[1] Christa Haldrup,[2] Jesper B. Bramsen,[2] Karina D. Sørensen,[2] Søren Høyer,[3] Torben F. Ørntoft,[2] Claus L. Andersen,[2] Michael L. Nielsen,[1] and Jesper V. Olsen[1,5,*]
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Cell (2019)

Functional mapping of differential signaling by RPTK mutants

Oncogenic Mutations Rewire Signaling Pathways by Switching Protein Recruitment to Phosphotyrosine Sites

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https://doi.org/10.1016/j.cell.2019.09.008

Nature Communications (2020)

Highest throughput, sensitivity, and scalability to date

ARTICLE

https://doi.org/10.1038/s41467-020-14609-1 OPEN

Rapid and site-specific deep phosphoproteome profiling by data-independent acquisition without the need for spectral libraries

Dorte B. Bekker-Jensen[1], Oliver M. Bernhardt[2], Alexander Hogrebe[1], Ana Martinez-Val[1], Lynn Verbeke[2], Tejas Gandhi[2], Christian D. Kelstrup[1], Lukas Reiter[2] & Jesper V. Olsen[1*]

Nature Communications (2021)

Subcellular compartmental proteomics

ARTICLE

https://doi.org/10.1038/s41467-021-27399-y OPEN

Spatial-proteomics reveals phospho-signaling dynamics at subcellular resolution

Ana Martinez-Val[1], Dorte B. Bekker-Jensen[1,2], Sophia Steigerwald[1,3], Claire Koenig[1], Ole Østergaard[1], Adi Mehta[4], Trung Tran[4], Krzysztof Sikorski[4], Estefanía Torres-Vega[5], Ewa Kwasniewicz[6], Sólveig Hlín Brynjólfsdóttir[7], Lisa B. Frankel[7,8,9], Rasmus Kjøbsted[10], Nicolai Krogh[11], Alicia Lundby[1,5], Simon Bekker-Jensen[6], Friðtjof Lund-Johansen[4✉] & Jesper V. Olsen[1✉]

Nature Communications (2021)

Clinically actionable resistance mechanisms

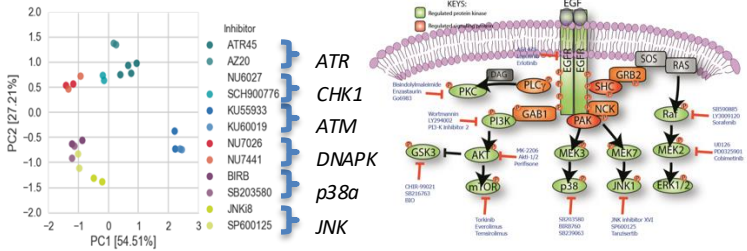
ARTICLE

https://doi.org/10.1038/s41467-021-22787-9 OPEN

Proteomics of resistance to Notch1 inhibition in acute lymphoblastic leukemia reveals targetable kinase signatures

Giulia Franciosa[1], Jos G. A. Smits[1,2], Sonia Minuzzo[3], Ana Martinez-Val[1], Stefano Indraccolo[3,4] & Jesper V. Olsen[1✉]

ONGOING (MULTICENTER): Profiling of DDR and core kinase pathway inhibitors (>45)



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- Lead and co-PI on numerous HGSOC &TNBC trials
- Lead PI on ACR-368 platinum-resistant ovarian trials

CLINICAL OVERVIEW OF PAST LILLY-SPONSORED MULTI-CENTER ACR-368 MONOTHERAPY STUDIES

Indication	Trial	ORR# (confirmed)	Median DoR°	Reference
HGSOC* (BRCA wild type and mutant; platinum-resistant and refractory)	Phase 2 (46-center, 8-country study)	12.1% (platinum-resistant)	5.6 months	Konstantinopoulos et al; Gynec. Oncol.: 2022
Squamous cell cancer (anal cancer, head & neck cancer [H&N])	Phase 1b multi-center	19% HPV+ H&N 15% anal cancer	7 months (HPV+ H&N) 12 months anal cancer	Hong et al, CCR, 2018

Dosing and Administration

- IV q14d (RP2D = 105 mg/m^2)

Safety summary

- Acceptable safety profile in >1,000 patients
  - No clinical or regulatory holds imposed across all clinical studies to date
- Primary adverse events ≥ grade 3 were hematological (manageable neutropenia and thrombocytopenia)
- Limited ≥ grade 3 non-hematological toxicities (≤7% for all AEs)
- Drug-related discontinuations <1-2%

Despite significant efforts, no predictive biomarkers were identified, need for alternative biomarker approach

*High grade serous ovarian cancer; # Overall response rate; °Duration of Response

OVARIAN CANCER TREATMENT LANDSCAPE BECOMING INCREASINGLY CROWDED

- ≥2nd line SOC segmented with 2 ADCs (Elahere and Enhertu), chemo (Doxyl, topotecan, gem) +/-Bev, and PARPi maintencance (BRCA mutated)
- Estimated new addressable cases of ≥2nd line platinum-resistant cancer cases ~7,600 (90% x60% x 14,000) new cases/year (excluding Elahere and Enhertu)
- > 10 emerging therapies, including ADCs, targeted agents (including DDRi), and various combinations

Exhibit 2 - Notable Ovarian Cancer Presentations at ESMO'24

Company	Drug	Modality	Target	Population	Abstract	Title
IMGN	Mirvetuximab	ADC	FRα	PSOC	718MO	Mirvetuximab soravtansine (MIRV) in recurrent platinum-sensitive ovarian cancer (PSOC) with high folate receptor-alpha (FRα) expression: Results from the PICCOLO trial
GMAB	Rina-S	ADC	FRα	Endometrial/ Ovarian	719MO	A phase I/II study of rinatabart sesutecan (Rina-S) in patients with advanced ovarian or endometrial cancer
STRO	Luveltamab tazevibulin	ADC	FRα	High-grade EOC	749P	Luveltamab tazevibulin, an antifolate receptor alpha (FRα) antibody-drug conjugate (ADC), in combination with bevacizumab (bev) in patients with recurrent high-grade epithelial ovarian cancer (EOC): STRO-002-GM2 phase I study
AZN	AZD5335	ADC	FRα	PRROC	754P	Initial results from a first-in-human study of AZD5335, a folate receptor α (FRα)-targeted antibody-drug conjugate, in patients (pts) with platinum-resistant recurrent ovarian cancer (PRROC)
Coherent Biopharma	CBP-1008	Bi-XDC	FRα/TRPV6	Solid tumors (PROC)	787P	First-in-human, phase I study of CBP-1008, a first-in-class bi-specific ligand drug conjugate (Bi-XDC), in patients with advanced solid tumors
IMGN	Mirvetuximab	ADC	FRα	FRα high OC	746P	Phase III MIRASOL trial: Updated overall survival results of mirvetuximab soravtansine (MIRV) vs. investigator's choice chemotherapy (ICC) in patients (pts) with platinum-resistant ovarian cancer (PROC) and high folate receptor-alpha (FRα) expression
AZN	Datopotamab	ADC	TROP-2	Endometrial/ Ovarian	714MO	Datopotamab deruxtecan (Dato-DXd) in patients with endometrial (EC) or ovarian cancer (OC): Results from the phase II TROPION-PanTumor03 study
MRK/Kelun	Sacituzumab tirumotecan	ADC	TROP-2	Endometrial/ Ovarian	715MO	Safety and efficacy of sacituzumab tirumotecan (sac-TMT) in patients (pts) with previously treated advanced endometrial carcinoma (EC) and ovarian cancer (OC) from a phase II study
Hengrui	SHR-A1921	ADC	TROP-2	PROC	717MO	SHR-A1921 in platinum-resistant ovarian cancer (PROC): data from a first-in-human (FIH) phase I study
TORL	TORL-1-23	ADC	CLDN6	Ovarian, endometrial, testicular	721MO	Phase I, two-part, multicenter first-in-human (FIH) study of TORL-1-23: A novel claudin 6 (CLDN6) targeting antibody drug conjugate (ADC) in patient with advanced solid tumors
Alphamab Oncology	JSKN003	ADC	HER2 x TOP1i	PROC	759P	JSKN003, a HER2-targeting antibody-drug conjugate, in patients with platinum-resistant ovarian cancer: A pooled analysis of two studies
IMCR	Brenetafusp	TCER	PRAME x CD3	PROC	750P	Phase I safety and efficacy of brenetafusp, a PRAME × CD3 ImmTAC T cell engager, in platinum resistant ovarian cancer (PROC)
INCY	INCB123667	Small molecule	CDK2	Advanced Solid tumours (49% OC)	617MO	Safety and tolerability of INCB123667, a selective CDK2 inhibitor, in patients (pts) with advanced solid tumors: A phase I study
ASND	TransCon IL-2 β/γ	IL-2 pro-drug + chemo	IL-2 β/γ-R	PROC	762P	First results from phase II dose expansion cohort of transcon IL-2 β/γ in combination with standard of care chemotherapy for platinum resistant ovarian cancer (PROC) in the IL Believe trial
BNTX/ OncoC4	Gotistobart	mAb	CTLA-4	PROC	LBA32	A randomized, phase II, dose optimization of gotistobart, a pH-sensitive anti-CTLA-4, in combination with standard dose pembrolizumab in platinum-resistant recurrent ovarian cancer: Safety, efficacy and dose optimization (PRESERVE-004/GOG-3081)
Hengrui	Fuzuloparib +apatinib	Small molecule combo	PARP/VEGF	Ovarian	766P	A phase II trial of fuzuloparib in combination with apatinib vs. fuzuloparib alone for recurrent ovarian cancer (OC)
Academic	Olaparib +cediranib	Small molecule combo	PARP/VEGF	PSOC	LBA33	ICON9: International phase III randomized study to evaluate the efficacy of maintenance therapy with olaparib and cediranib or olaparib alone in patients with relapsed platinum-sensitive ovarian cancer following a response to platinum-based chemotherapy
Other Notable/Long-Term Maintenance Studies						
GSK	Niraparib	Chemo	PARP	Newly-diagnosed advanced OC	LBA29	Final overall survival (OS) in patients (pts) with newly diagnosed advanced ovarian cancer (aOC) treated with niraparib (nir) first-line (1L) maintenance: Results from PRIMA/ENGOT-OV26/GOG-3012
Pharma&/ GmbH	Rucaparib+ nivo	Chemo+IO	PARP/PD-1	Newly-diagnosed advanced OC	LBA30	ATHENA-COMBO, a phase III, randomized trial comparing rucaparib (RUCA) + nivolumab (NIVO) combination therapy vs RUCA monotherapy as maintenance treatment in patients (pts) with newly diagnosed ovarian cancer (OC)
Academic	Ganetespib +carboplatin	Small molecule combo	DNA repair inhibition	Ovarian	LBA34	ENGOT-ov48/EUDARIO: European trial on enhanced DNA repair inhibition in ovarian cancer

Source: Jefferies research; ESMO 2024

APRIL 2024 UPDATE: PROSPECTIVE ONCOSIGNATURE RESPONSE PREDICTION (CONFIRMED ORR 50%) IN GYN CANCER PATIENTS

Registrational intent Phase 2b trial

Overall Response	Total[1]			Ovarian		Endometrial	
	BM+ Monotherapy	BM- LDG Combination	Total	BM+ Monotherapy	BM- LDG Combination	BM+ Monotherapy	BM- LDG Combination
	N = 10	N = 16	N=26	N = 5	N = 11	N = 5	N = 5
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
CR	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
cPR	5 (50)	0 (0)	5 (19)	2 (40)	0 (0)	3 (60)	0 (0)
uPR	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SD	3 (30)	8 (50)	11	2 (40)	6 (55)	1 (20)	2 (40)
PD	2 (20)	8 (50)	10	1 (20)	5 (45)	1 (20)	3 (60)
cORR (95% CI)	**50.0%**	**0%**	**19.2%**	**40% (12, 77)**	**0%**	**60% (23, 88)**	**0%**
OncoSignature BM+ vs BM- Segregation P = 0.0038				**P = 0.083**		**P = 0.083**	

[1]Subjects with ≥1 on-treatment scan

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

Data cut as of 1 April 2024

BLINDED KOL MARKET RESEARCH UNDERSCORES ENDOMETRIAL CANCER REPRESENTS SIGNIFICANT OPPORTUNITY FOR ACR-368 (US NUMBERS)

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

- 2L now of high unmet need and opportunity for accelerated single agent approval
  - **90% of cases believed to progress to 2L therapy (~27,000 patients in the US/year)**
  - Recent front-line approvals of anti-PD-1 plus chemo[1,2] for high grade EC reduces/eliminates pembro + lenvatinib[3] as viable 2L option for most patients
  - **Reported chemotherapy efficacy in 2L : ORR = 10-15% and mPFS = 2.8 – 3.8 months][3,4]**
  - Limited number of early emerging therapies; Enhertu approved for ~15% of Her2(+++)

- 1L potential opportunity for label expansion in confirmatory trial (maintenance with ACR-368 + anti-PD-1)
  - **New cases of high grade, recurrent EC (progressed on ICI + chemo) ~30K patients/year**
  - Leverage ACR-368 clinical activity in patients progressing on prior anti-PD-1 therapy and anti-PD-1 combo synergy
  - **mPFS in anti-PD-1 maintenance phase ~9 months in pMMR (>27 months in dMMR)**

*SEER database

[1]Eskander et al, NEJM 2023; [2]Mirza et al, NEJM 2023; [3]Makker et al, NEJM 2022; [4]Ray-Coquard I et al, BJC, 2013

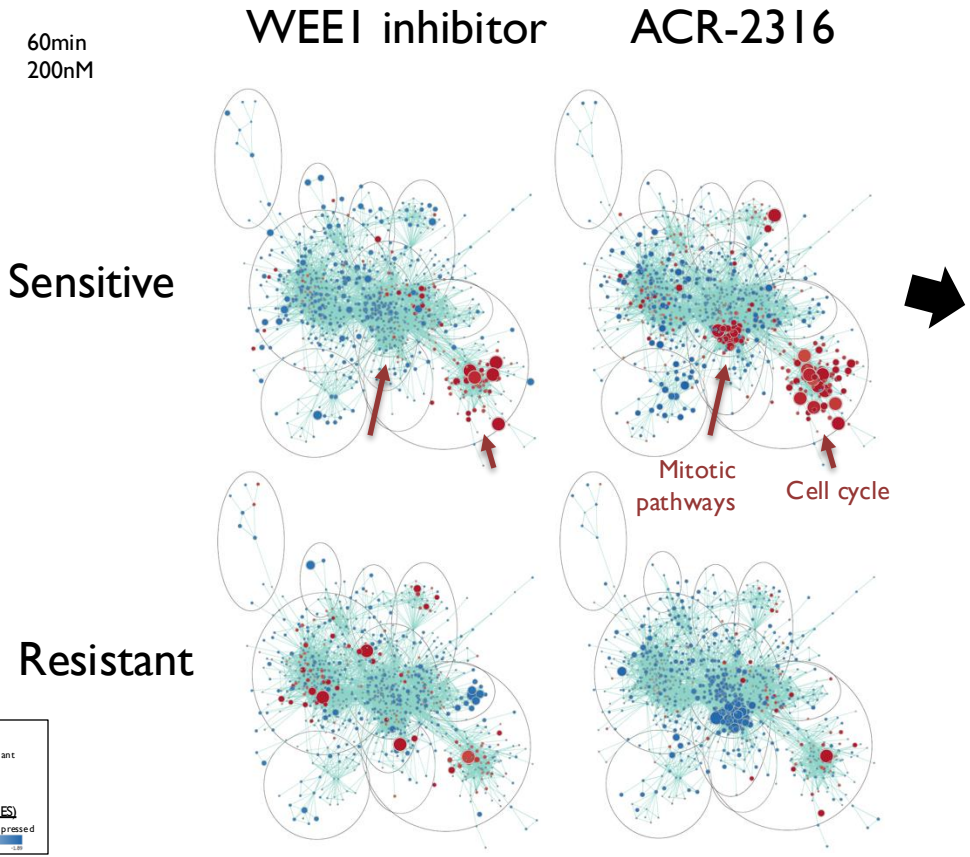
DEMOGRAPHICS AND SUBJECT DISPOSITION—ENDOMETRIAL SUBJECTS (N=35)

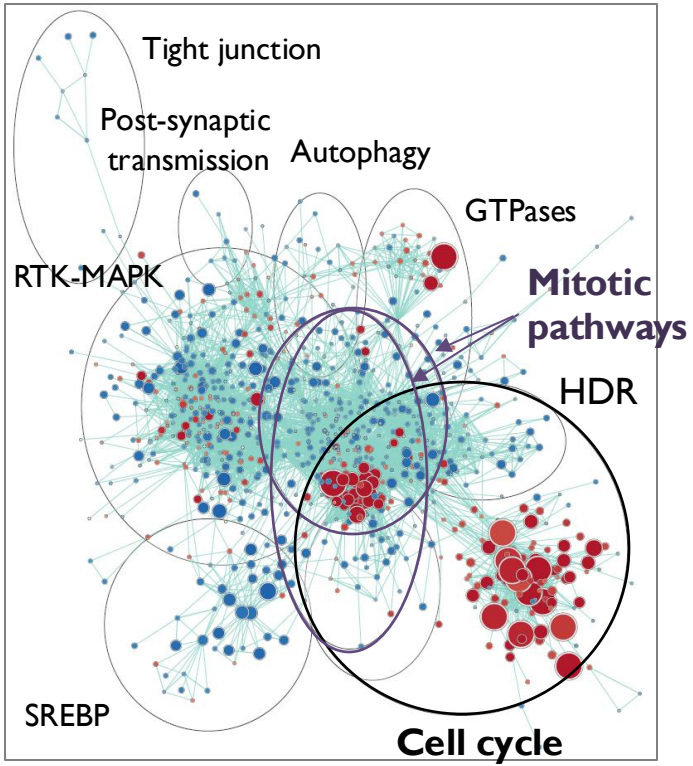
Subject Demographics	BM+ N = 12	BM- N = 23
Median Age (range)	66 (60-76)	68 (42-78)
Race (%)		
White	8 (67)	16 (70)
Black/African American	3 (25)	3 (13)
Asian	0 (0)	3 (13)
Other	0 (0)	1 (4)
Unknown	1 (8)	0 (0)
Current Stage (%)		
III	3 (25)	12 (52)
IV	9 (75)	10 (43)
unk	0 (0)	1 (4)
Histology (%)		
Serous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

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

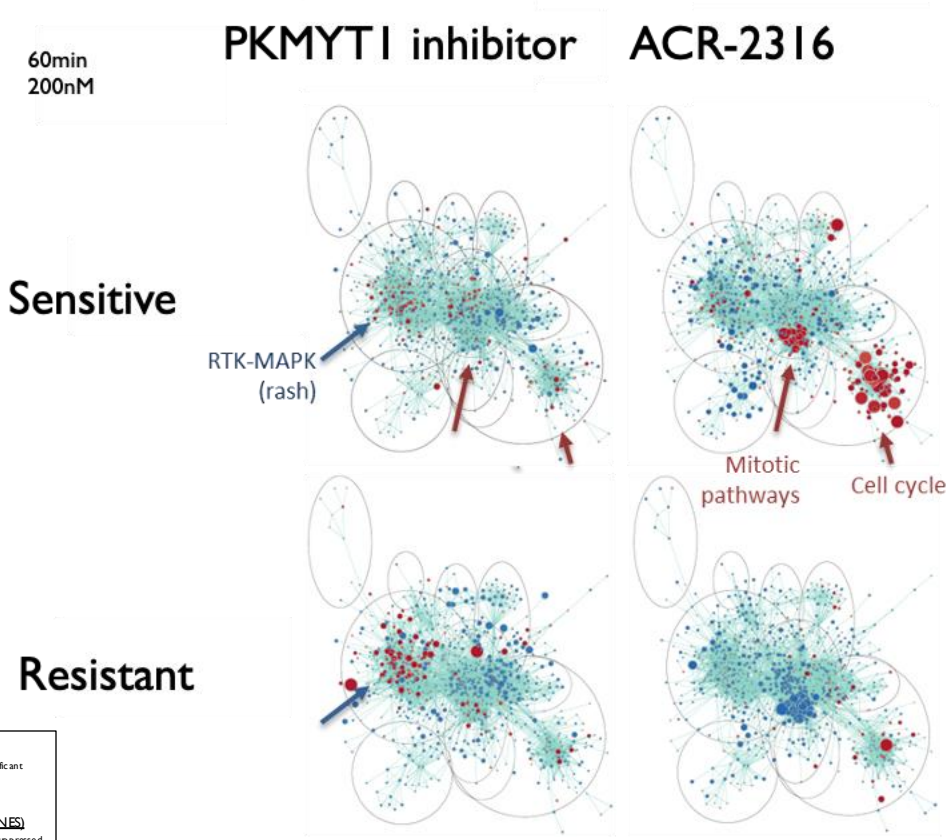
*Subject deemed ineligible for anti-PD-1 therapy.
^1 BM+ and 4 BM- subjects are still on study for follow-up, but no longer receiving study drug.
Data current as of 25July2024 and includes all subjects enrolled with registrational intent
BM- includes all subjects treated with ACR-368 + low dose gemcitabine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

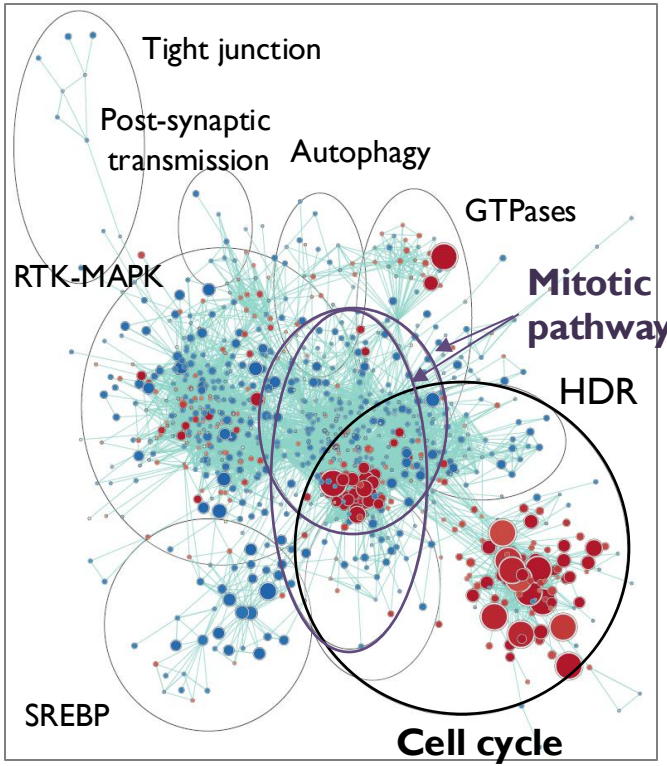
AP3 ANALYSIS: ACR-2316 REGULATES CELL CYCLE AND MITOSIS MORE POTENTLY THAN BENCHMARK WEE1 INHIBITOR



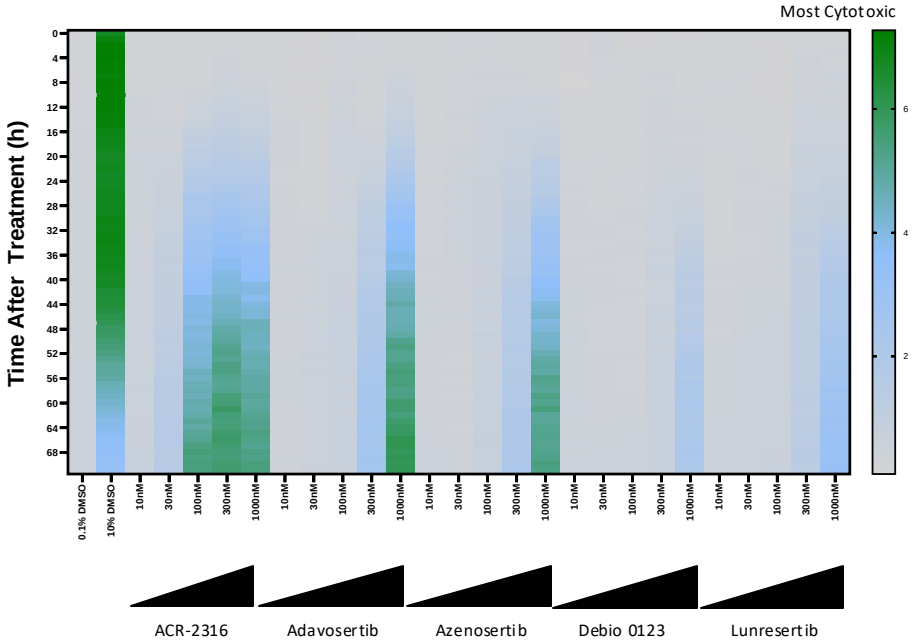


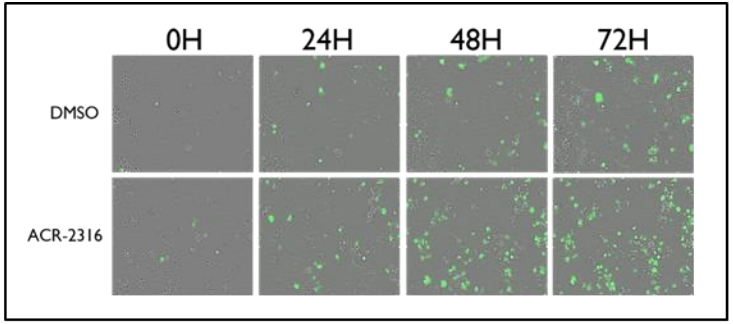
AP3 ANALYSIS: ACR-2316 REGULATES CELL CYCLE AND MITOSIS MORE POTENTLY THAN BENCHMARK PKMYT1 INHIBITOR





ACR-2316 INDUCES POTENT CELL DEATH COMPARED TO BENCHMARK WEE1 AND PKMYT1 INHIBITORS

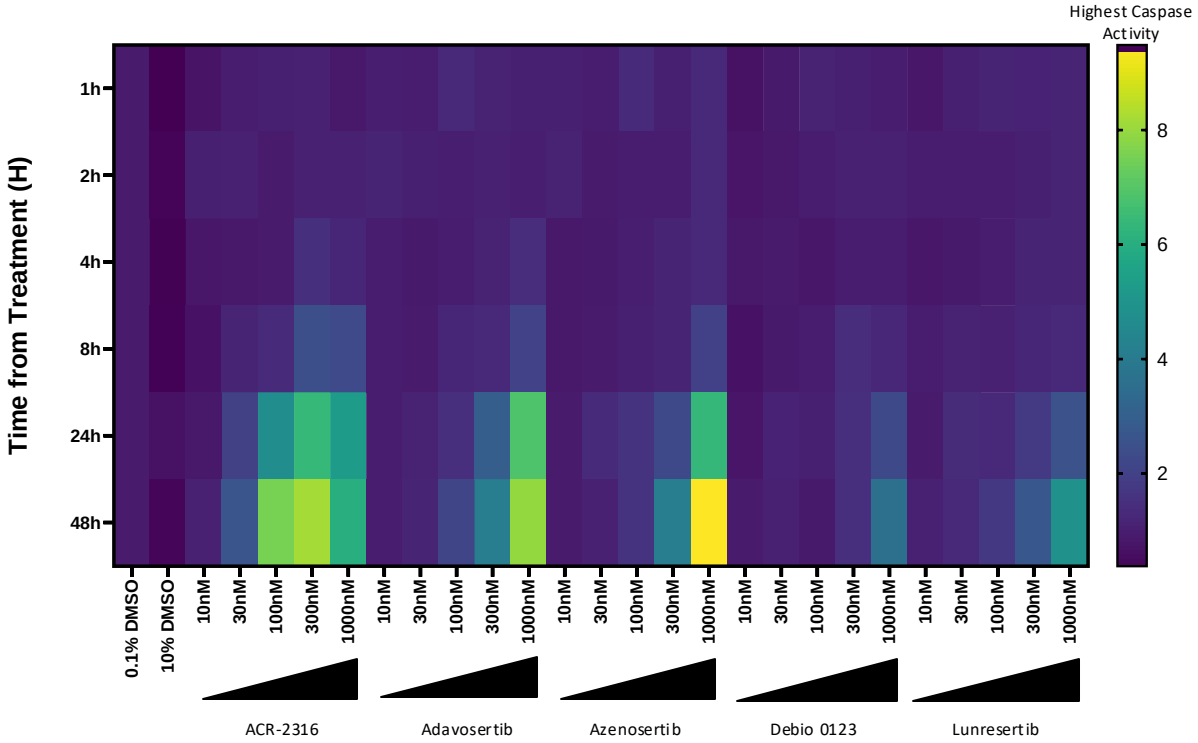




Representative images of OVCAR3 cells treated with 0.1% DMSO or 100 nM ACR-2316 (green fluorescence = dead cells)

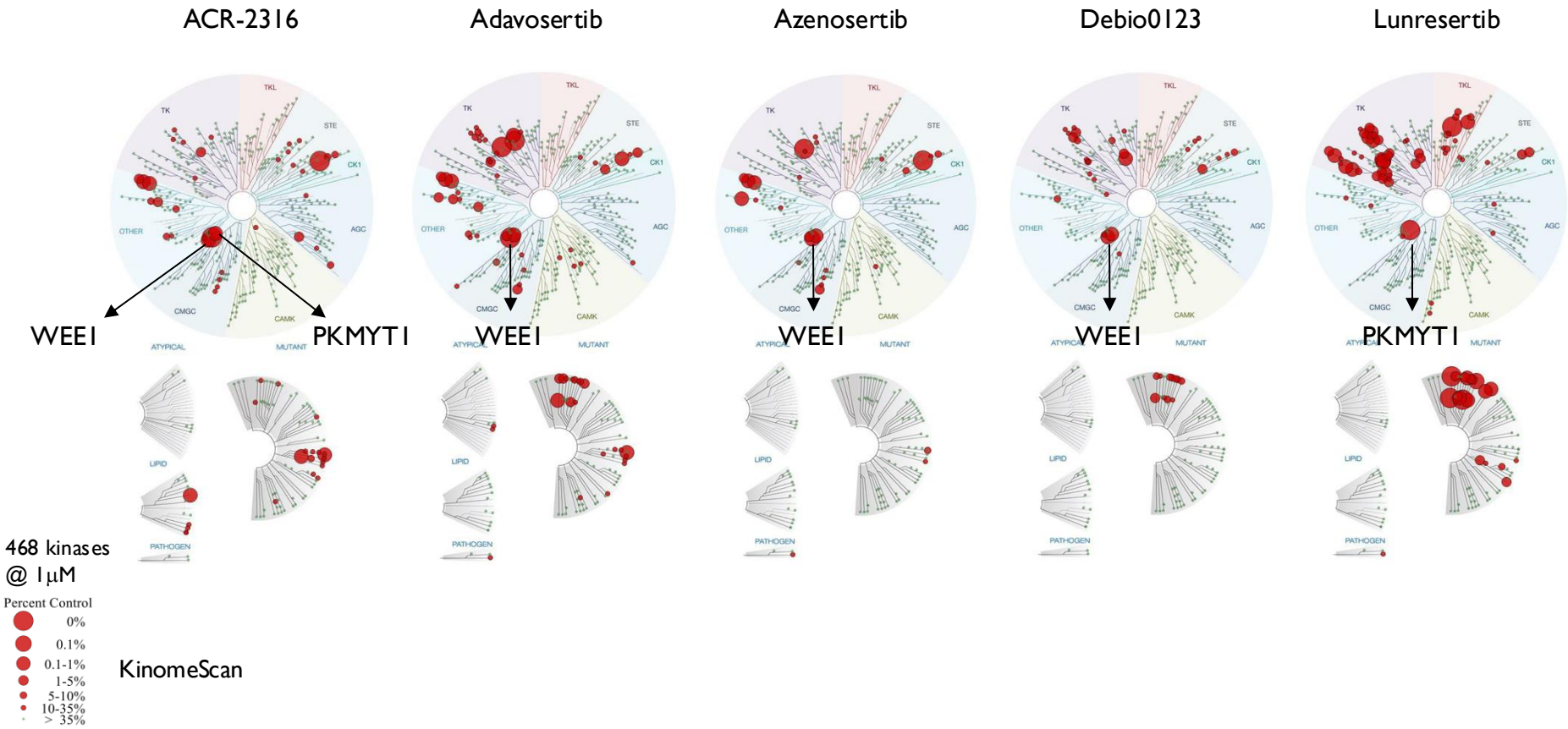
CellTox-Green Assay

ACR-2316 INDUCES POTENT CASPASE 3/7 CLEAVAGE COMPARED TO BENCHMARK WEE1 OR PKMYT1 INHIBITORS



Caspase 3/7-Glo Assay

COMPREHENSIVE KINOME SELECTIVITY PROFILING



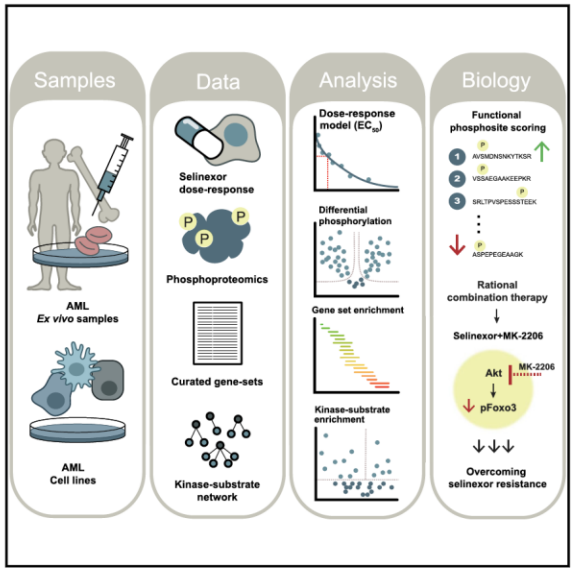
AP3 REVEALS SINGLE AGENT SENSITIVITY CONTEXT AND RATIONAL DRUG COMBINATIONS INDEPENDENT OF GENETIC INFORMATION

Article

Cell Reports

Phosphoproteomics of primary AML patient samples reveals rationale for AKT combination therapy and p53 context to overcome selinexor resistance

Graphical abstract



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In brief

Emdal et al. combine phosphoproteomics of samples from patients with AML and functional phosphosite scoring to uncover clinically actionable molecular context for selinexor efficacy. Sensitivity to selinexor correlates with functional p53 and is enhanced with nutlin-3a, while resistance is associated with dysregulated AKT-FOXO3 signaling and overcome by combining with MK-2206.

Using spatial phosphoproteomics (*Nat. Commun.*, 2021) Acrivon's AP3 platform can uncover single agent sensitivity and rational drug combinations for targets with complicated mechanism of action

Cell Reports, August 9, 2022

ELI LILLY ACR-368 HIGH LEVEL LICENSE TERMS (RIGHT OF FIRST NEGOTIATION)

- In-licensing completed 27 January 2021
  - WW exclusive rights with rights to sub-license
  - $5M up front and low single digit percentage equity subject to ordinary dilution going forward
  - Aggregate development and commercial milestone payments of up to $168M, of which $5M is due prior to NDA
  - Tiered percentage royalty on annual net sales ranging from low single-digit up to a maximum of 10% subject to certain specified reductions
  - Drug product as well as drug substance sufficient to treat several hundred patients
  - Limited right of first negotiation expiring 45 days upon completion of certain clinical milestones