Acrivon Therapeutics

ACRIVON PREDICTIVE PRECISION PROTEOMICS (AP3)

OVERCOMING LIMITATIONS OF GENETICS-BASED PRECISION MEDICINE

CORPORATE PRESENTATION

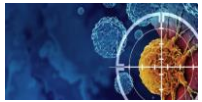
AUGUST 2024

FORWARD-LOOKING STATEMENTS

Certain information contained in this presentation includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations. In some cases, you can identify forward-looking statements because they contain words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," or "would" or the negative of these words or other similar terms or expressions. Our forward-looking statements are based primarily on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and results of operations. The outcome of the events described in the forward-looking statements is subject to risks and uncertainties, including the factors described in our filings with the U.S. Securities and Exchange Commission. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this presentation. The results, events, and circumstances reflected in the forward-looking statements may not be achieved or occur, and actual results, events, or circumstances could differ materially from those described in the forward-looking statements.

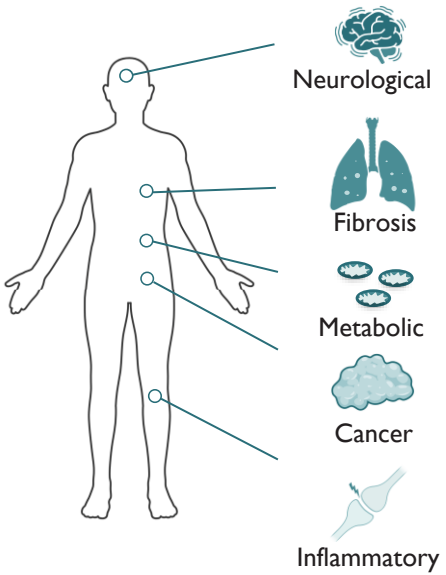
You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this presentation. We undertake no obligation to update any forward-looking statements or to reflect new information or the occurrence of unanticipated events, except as required by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

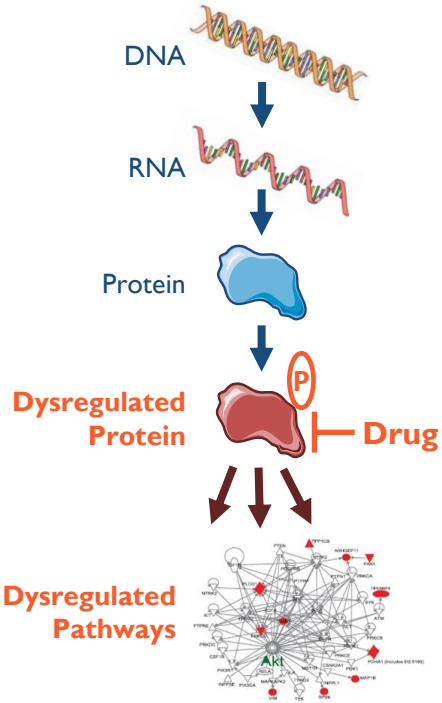
CRITICAL CHALLENGES FACING BIOPHARMA INDUSTRY

	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

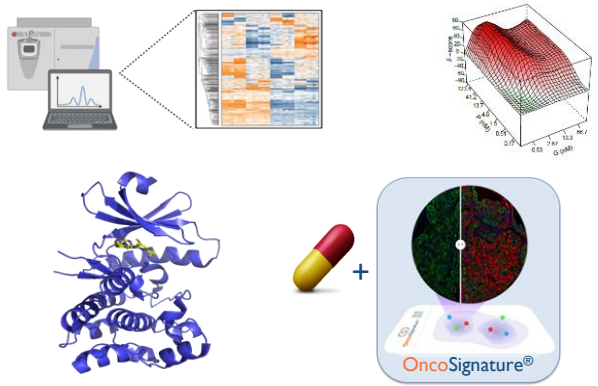
ACRIVON THERAPEUTICS – A NEXT-GENERATION PRECISION MEDICINE COMPANY





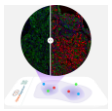
Acrivon Predictive Precision Proteomics (AP3)

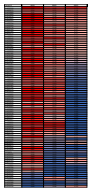
- Enables an exact match between the disease-driving, dysregulated pathways with a drug's mechanism of action (Acrivon meaning ≈ exact, accurate)
- Broadly applicable in R&D (biological SAR, resistance, patient responders); leveraged for internal pipeline

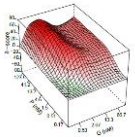


Blume-Jensen, P &Hunter, T: Oncogenic kinase signaling *Nature* (2001)
Olsen, JV et al: Global, in vivo, and site-specific phosphorylation dynamics in signaling networks *Cell* (2006);
Andersen, JN et al: Pathway-based identification of biomarkers for targeted therapeutics: personalized oncology with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

AP3: HIGHLY DIFFERENTIATED - MULTIPLE R&D DELIVERABLES







Clinical Biomarkers
Predictive OncoSignature tests

Indication Finding
Sensitive tumor types

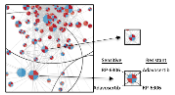
Resistance Mechanisms
Rational drug combinations

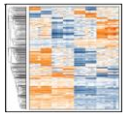
AP3

Drug Discovery SAR
Optimal target selectivity

PD Markers
~6,000 per compound

Informs in-licensing
AP3 profiling of candidates

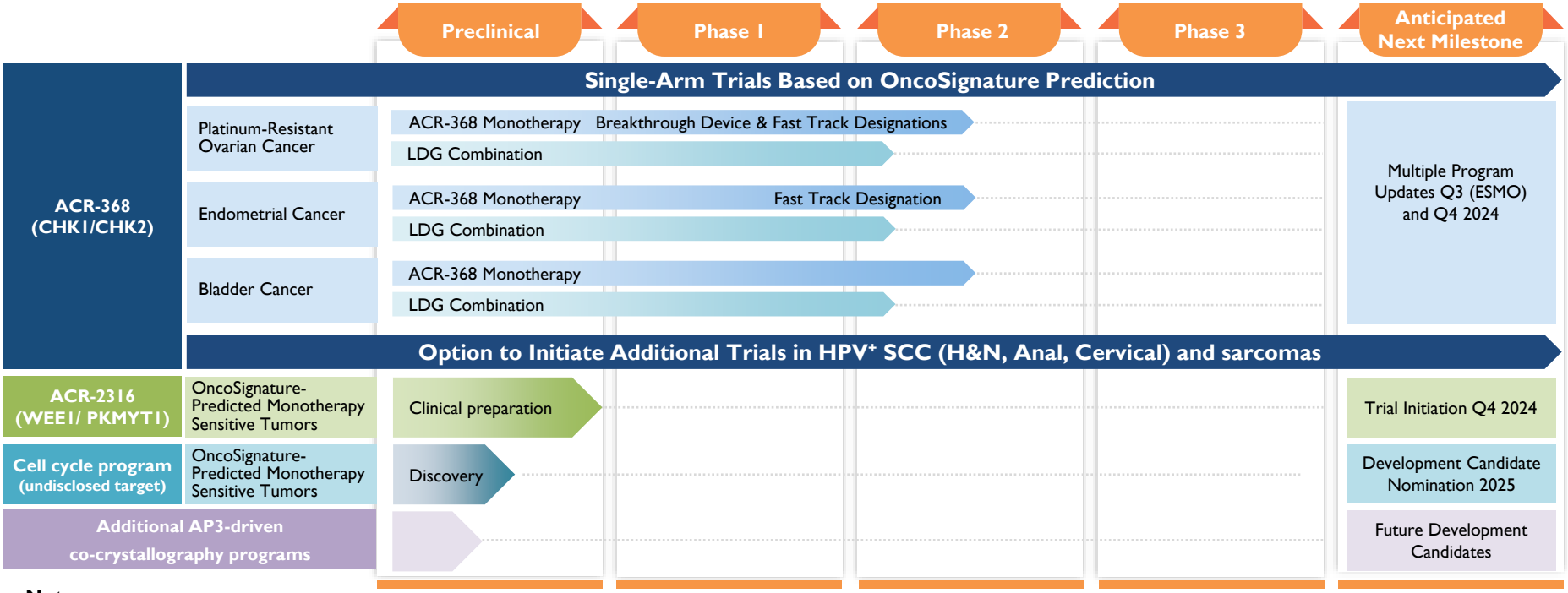




Intellectual Property
De novo exclusivity & protection against generics

Predicted Responder

ACRIVON PIPELINE



Notes

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

ACRIVON THERAPEUTICS FOUNDATION

Development Site (Boston)

- Drug and clinical biomarker assay development
- Clinical trials
- Market access pending approval

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
CEO, President, Co-Founder

Kristina Masson
EVP, Bus Ops, Site Head and Co-Founder

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

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

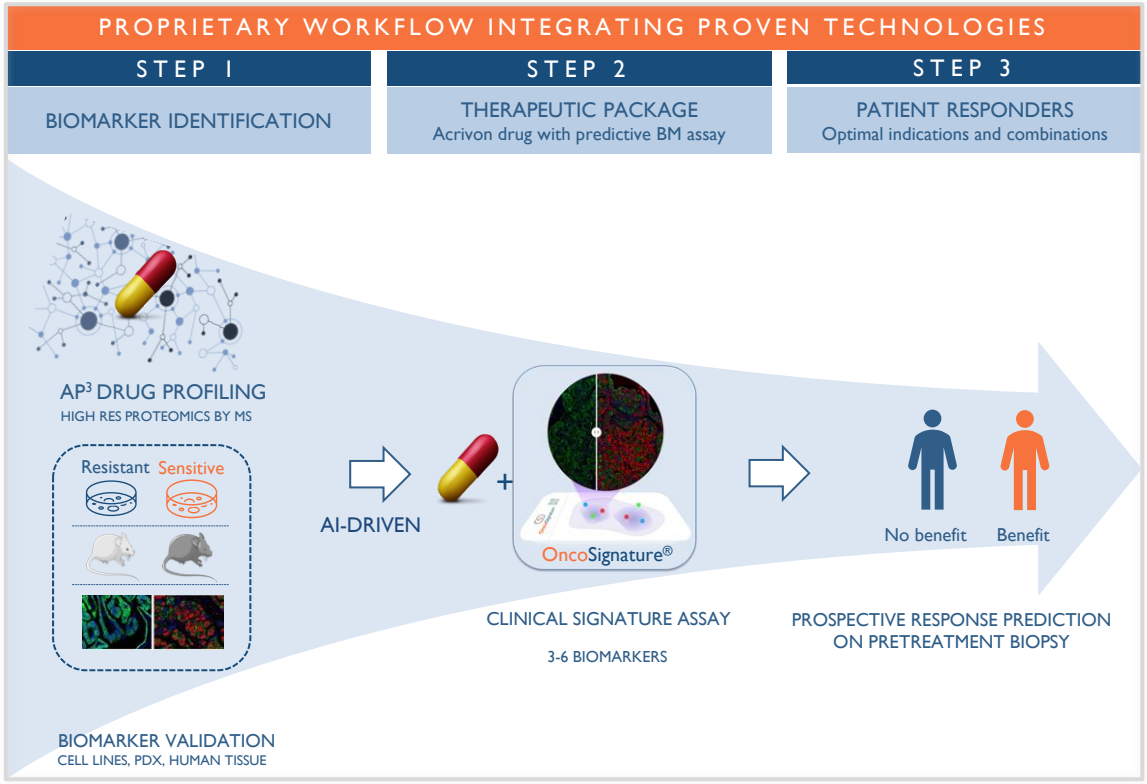
Erick Gamelin, M.D., Ph.D.
Chief Development Officer

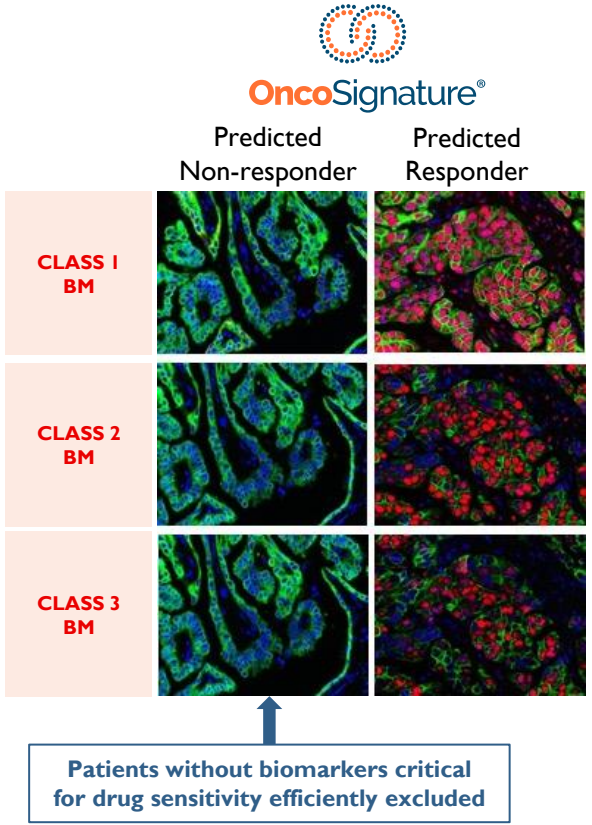
- Professor, CEO, large national cancer center and hospital
- Executive Amgen, Pfizer, Dynavax, MacroGenics; CMO STEP Pharma
- >100 ph 1-3 oncology trials

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”

AP3 PLATFORM: DRUG RESPONSE PREDICTION IN INDIVIDUAL PATIENTS

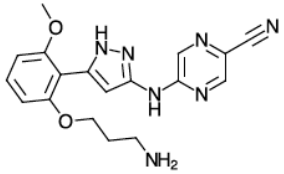




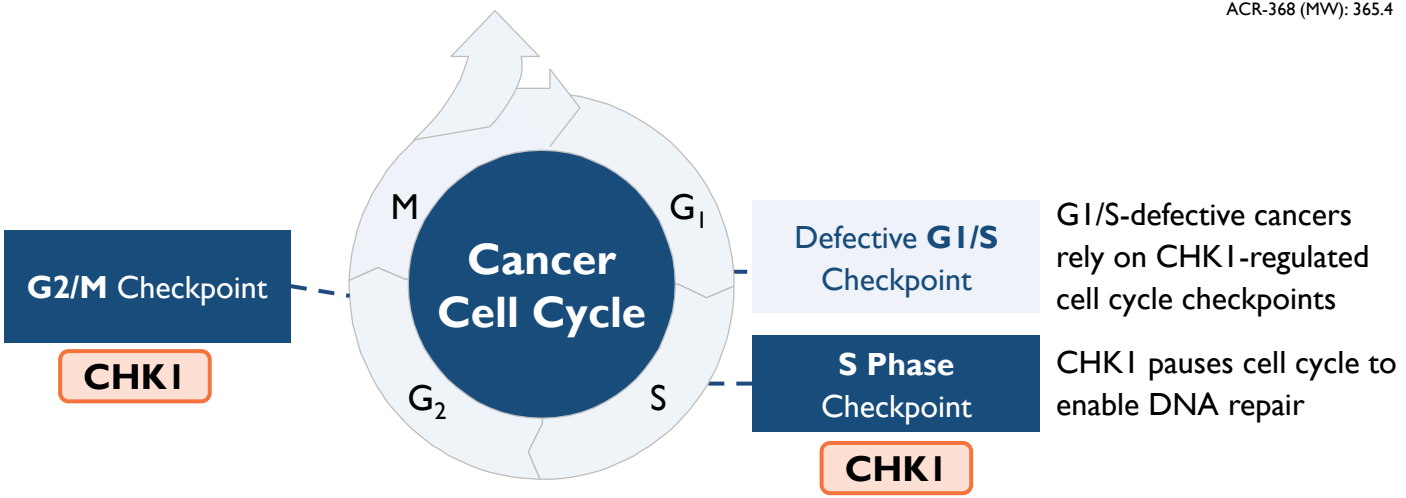
"Disease Pathway-Based Method to Generate Biomarker Panels Tailored to Specific Therapeutics for Individualized Treatments": EP 2 229 589, issued June 10, 2015; US2017/0067877A9, pending. OncoSignature® *is a Registered Trademark: US Reg. No. 5,718,472; Int. Cl. 5, 42. Intl. Reg. 1382289*

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

- ATP-competitive inhibitor of CHK1 (0.9 nM) and CHK2 (8 nM)
- Good ADME properties, minimal drug-drug interaction (DDI) potential
- Discovered by Array Biopharma, acquired by Eli Lilly & Company
- CoM patent exp. Oct., 2030; Salt-form exp. Apr., 2037



ACR-368 (MW): 365.4



G1/S-defective cancers rely on CHK1-regulated cell cycle checkpoints

CHK1 pauses cell cycle to enable DNA repair

- **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

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%

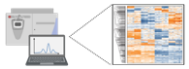
Despite significant efforts, no predictive biomarkers were identified, need for alternative biomarker approach

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

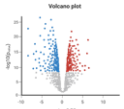
DEVELOPMENT OF AP3-BASED PATIENT SELECTION ONCOSIGNATURE TESTS

P-proteomics

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



Drug-regulated phospho-sites and biological processes

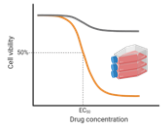


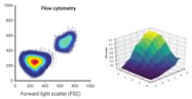
Pathway visualization and reconstitution

Literature and database mining

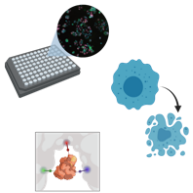
Cellular MOA

Dose response, knockdowns, drug combinations



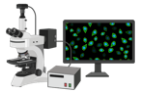


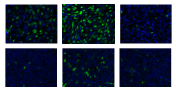
Target engagement, cell assays, imaging

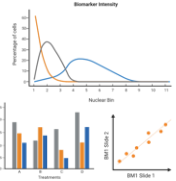


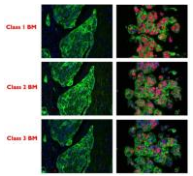
Technical Validation (Intended use tissue)

BM antibody validation by quantitative IF on human and PDX samples

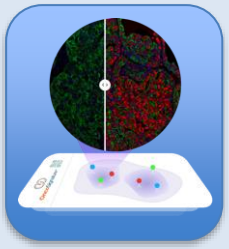








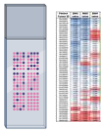
Final OncoSignature Assay



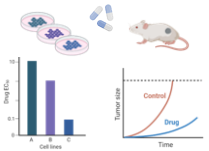
OncoSignature®

Functional Validation (Intended use tissue)

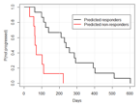
Human cancer screening: ID of drug-sensitive cancers and proportions of responders



Prediction of drug sensitivity in cancer cell lines and PDX models

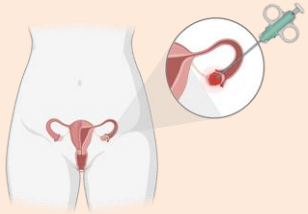


Patient responder prediction on pre-treatment tumor biopsies

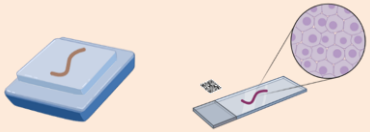


ACR-368 ONCOSIGNATURE TEST: USAGE IN THE CLINIC

Pretreatment tumor biopsy

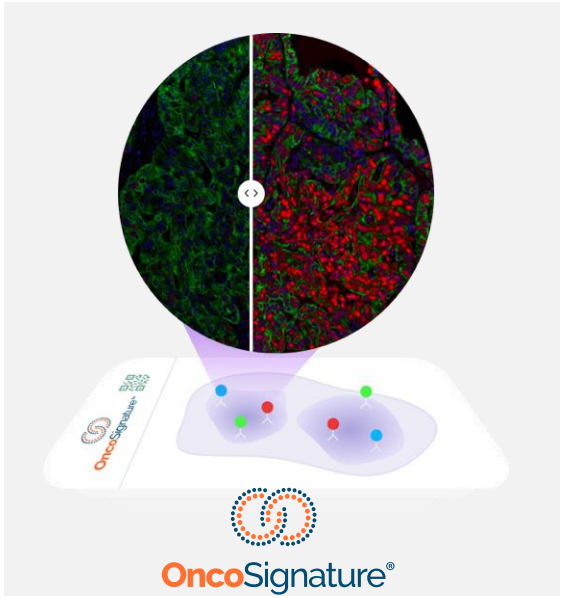


Sample processing



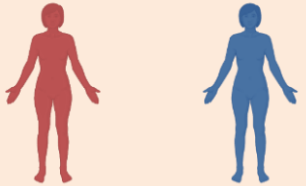
Biopsy in FFPE block

Automated tumor Region-of-Interest biomarker scoring



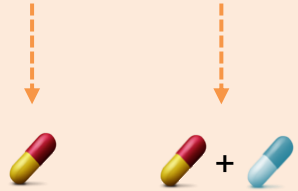
- Pretreatment tumor biopsy test
- Compatible with 5 business days turn-around
- Offered by CDx partner under exclusive license from Acrivon

Treatment decision based on patient stratification



OncoSignature-positive

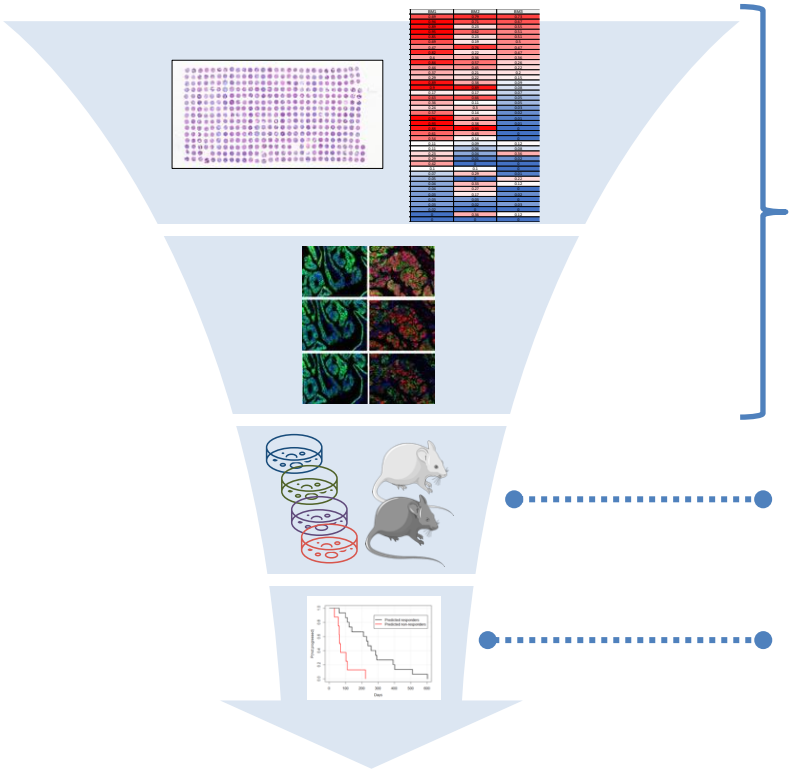
OncoSignature-negative



ACR-368 monotherapy

ACR-368 + LDG combination

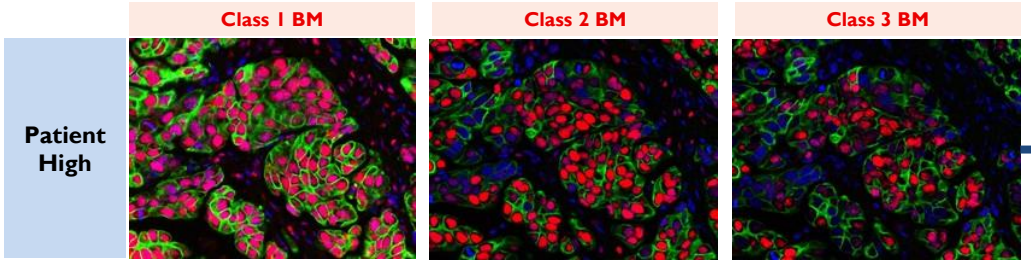
CONSISTENT ACR-368 ONCOSIGNATURE PERFORMANCE ACROSS PRECLINICAL STUDIES



OncoSignature®

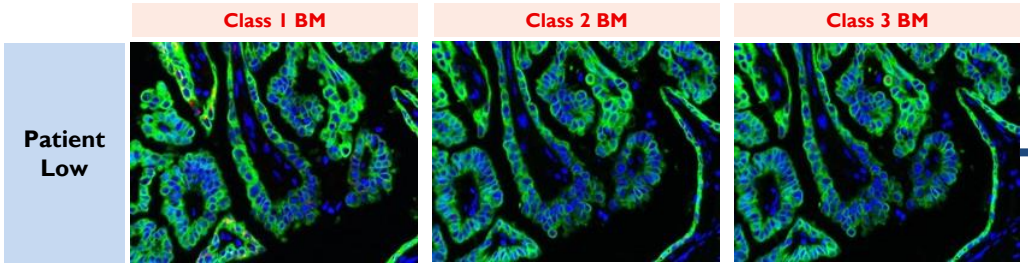
- Prediction of the fraction of human tumors sensitive to single agent ACR-368
  - Selection rate 30-40% across lead indications
- Identification of additional human tumor types predicted sensitive to single agent ACR-368
  - Endometrial and bladder cancer
- Prediction of treatment outcome in human PDX models
  - ORR enrichment to ≥ 55%; AUC of 0.88 and 0.9
- Two separate, prospectively designed, blinded studies of biopsies from past Phase 2 trials with ACR-368 in patients with platinum-resistant ovarian cancer
  - ORR enrichment to 47% (NCI) and 58% (Lilly multi-center)

ACR-368 ONCOSIGNATURE PREDICTION OF DRUG SENSITIVITY: BIOMARKER QUANTITATION ACROSS HUMAN CANCER PATIENT SAMPLES



Predicted Responder
Patient with drug target dependency

OncoSignature®

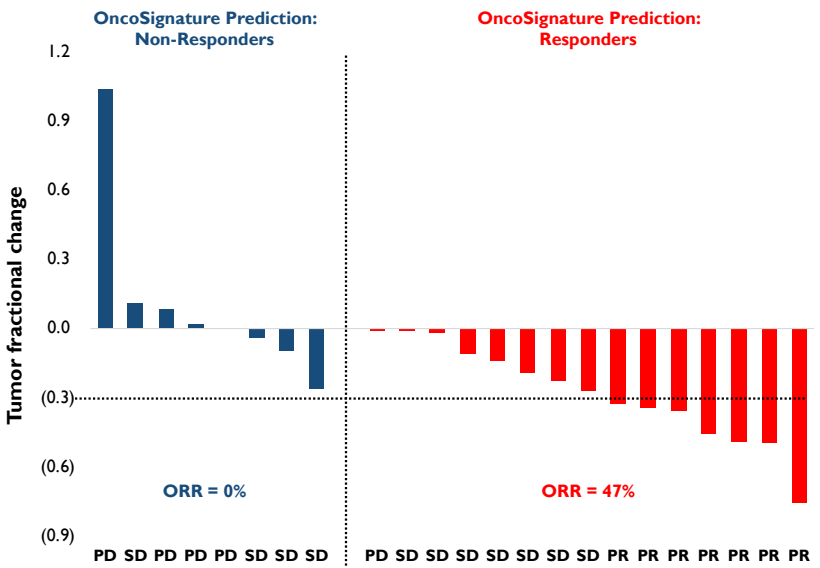


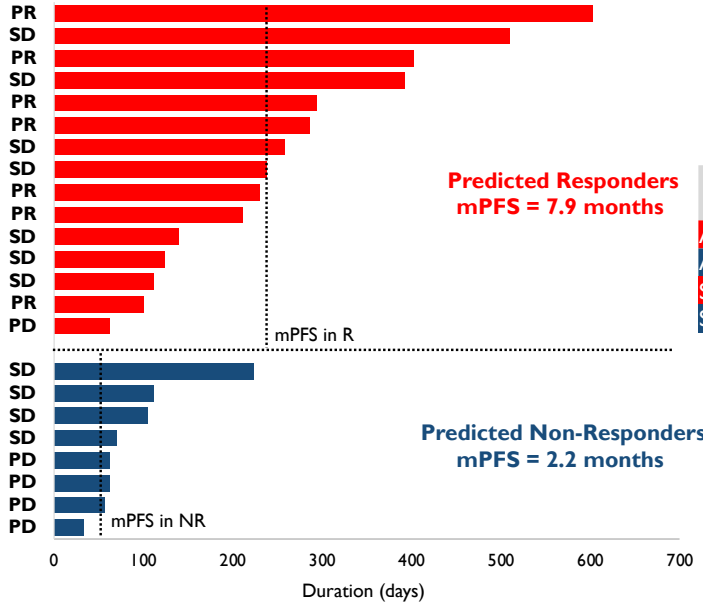
Predicted Non-Responder
Patient with no drug target dependency efficiently excluded

Tissue ID.	BM1	BM2	BM3
Fov060265	0.69	0.79	0.73
Fov050855	0.94	0.71	0.67
Fov041300	0.89	0.23	0.55
Fov060380	0.95	0.62	0.51
Fov060050	0.85	0.23	0.51
Fov041285	0.69	0.19	0.5
Fov100142	0.47	0.76	0.47
Fov050764	0.82	0.22	0.47
Fov041267	0.4	0.36	0.36
Fov100146	0.84	0.57	0.26
Fov060382	0.44	0.45	0.22
Fov041269	0.37	0.21	0.2
Fov060302	0.29	0.22	0.15
Fov020067	0.89	0.38	0.09
Fov100003	0.9	0.89	0.08
Fov050700	0.17	0.17	0.07
Fov050139	0.63	0.66	0.05
Fov041138	0.36	0.11	0.05
Fov060152	0.24	0.3	0.03
Fov030062	0.57	0.14	0.02
Fov060133	0.94	0.43	0.01
Fov050666	0.93	0.38	0.01
Fov060371	0.88	0.93	0
Fov020497	0.61	0.43	0
Fov010706	0.54	0.14	0
Fov020386	0.11	0.09	0.12
Fov050734	0.11	0.06	0.08
Fov040872	0.23	0.04	0.36
Fov050659	0.29	0.01	0.02
Fov060293	0.42	0	0
Fov060210	0.1	0.1	0
Fov050840	0.07	0.29	0.01
Fov040855	0.05	0	0.22
Fov050816	0.04	0.33	0.12
Fov060355	0.04	0.27	0
Fov010252	0.03	0.17	0.02
Fov010682	0.03	0.03	0
Fov060553	0.03	0.02	0.03
71768C3	0.02	0	0
Fov150230	0	0.36	0.12
Fov060308	0	0	0

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	0.96	0.66	0.73
Fov060075	0.54	0.51	0.38
Fov020069	0.31	0.30	0.38
Fov010809	0.34	0.16	0.36
Fov030970	0.93	0.28	0.33
Fov010892	0.95	0.72	0.32
Fov040102	0.98	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	0.77	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	0.82	0.14
Fov020160	0.58	0.30	0.14
Fov010252	0.86	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
Fov110004	0.90	0.36	0.05
Fov060003	0.78	0.24	0.05
Fov020061	0.87	0.20	0.05
Fov041269	0.70	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	0.81	0.00
Fov060434	0.93	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
Fov020262	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
Fov040624	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	0.08
Fov020002	0.57	0.06	0.08
Fov020111	0.16	0.05	0.11
Fov040872	0.31	0.04	0.01
Fov050666	0.98	0.03	0.00
Fov050659	0.81	0.03	0.03
A176RC1	0.44	0.03	0.05
Fov050555	0.20	0.02	0.01
Fov020193	0.89	0.02	0.10
Fov031530	0.81	0.01	0.10
Fov030763	0.59	0.01	0.29
Fov012115	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	0.05
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

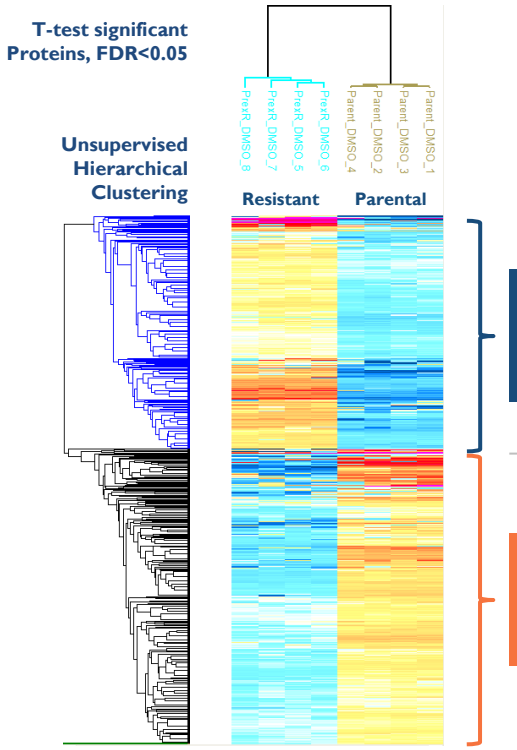
OncoSignature-positive = 30-50%

Endometrial cancer

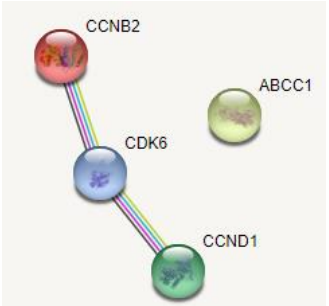
Tissue ID	BM1	BM2	BM3
Fur021904	0.16	0.38	0.86
Fur021989	0.86	0.17	0.71
Fur021785	0.14	0.55	0.69
Fur021984	0.87	0.62	0.63
Fur021937	0.81	0.65	0.61
Fur022037	0.12	0.22	0.54
Fur130035	0.55	0.48	0.50
Fur030113	0.90	0.65	0.31
Fur020288	0.60	0.26	0.30
Fur020281	0.21	0.57	0.27
Fur130010	0.79	0.75	0.27
Fur021781	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%

AP3 UNCOVERS ACTIONABLE ACR-368 RESISTANCE MECHANISMS UNBIASED AND INDEPENDENT OF GENETIC INFORMATION

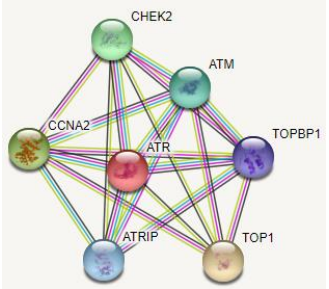


Upregulated in ACR-368 Resistant Cells



G1/S CELL CYCLE

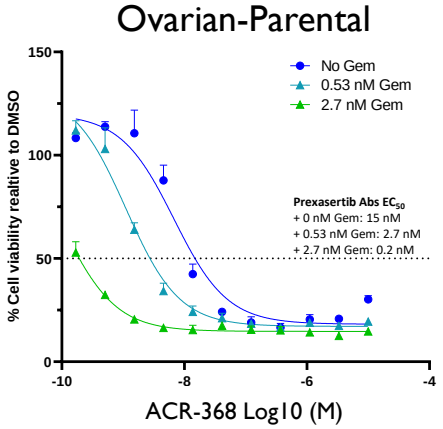
Downregulated in ACR-368 Resistant Cells

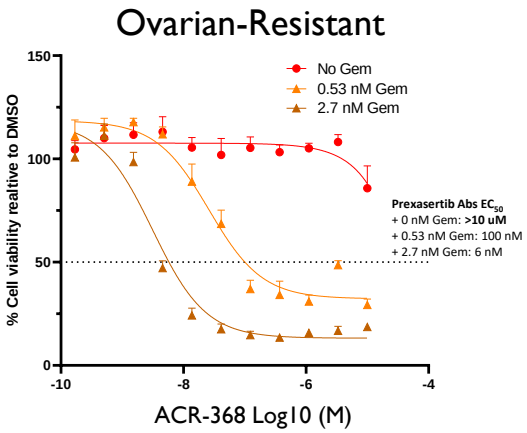


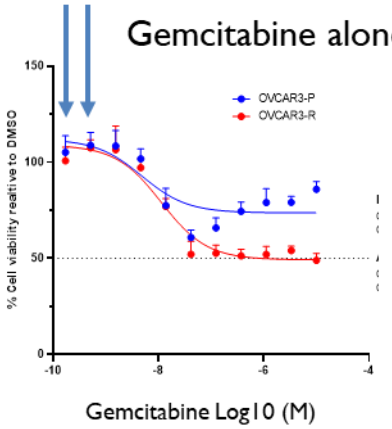
DNA DAMAGE REPAIR

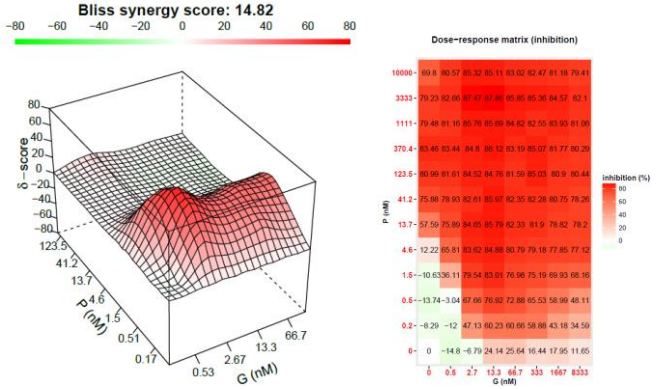
Data suggest that gemcitabine might be a rational combination to overcome DDR suppression

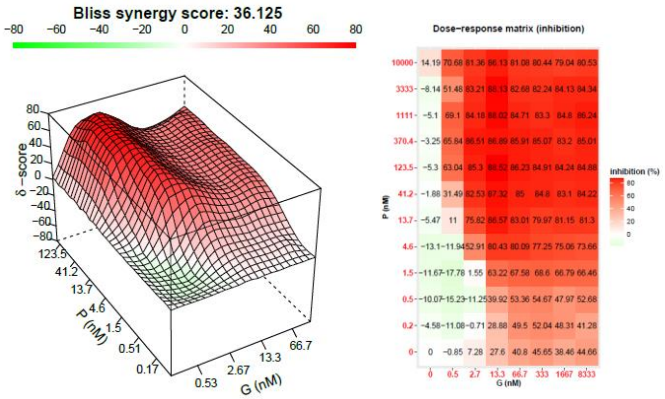
LOW DOSE GEMCITABINE SENSITIZES OVARIAN CANCER CELL LINES TO ACR-368











Bliss Synergy score:

- <-10: Drug interaction is likely antagonistic
- -10 to 10: Drug interaction is likely additive
- >10: Drug interaction is likely synergistic

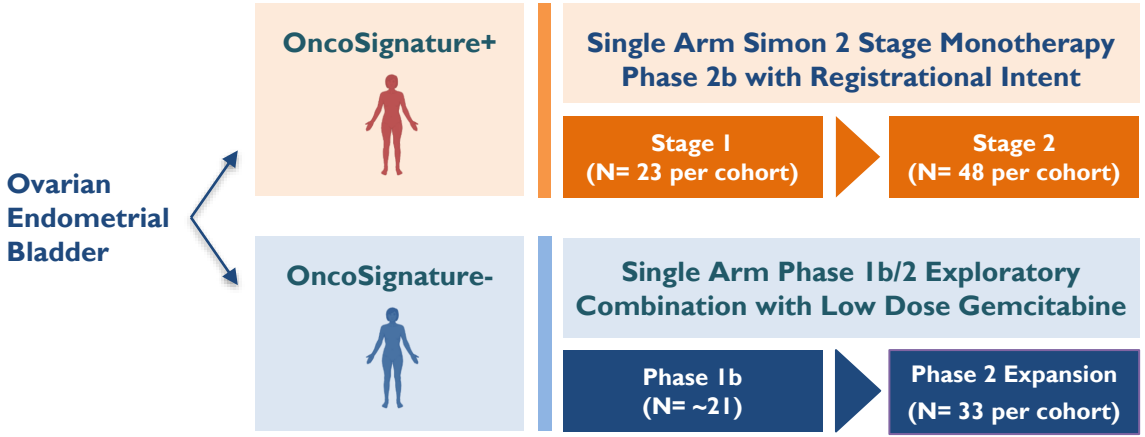
THERAPEUTIC BAR FOR HIGH GRADE PLATINUM-RESISTANT OVARIAN AND ENDOMETRIAL CANCER NEW APPROVALS

- Platinum-resistant ovarian cancer: ≥2nd line SOC* ~12% ORR, mDoR 3.7 – 5.7 months
  - Mirvetuximab: Post 1-3 prior lines, FRa-high PROC (~35% of patients; ORR ~35%, PFS = 5.6 months)
  - ~85% of patients with PROC do not benefit from mirvetuximab
- High grade endometrial cancer: ≥3rd line SOC** ~9% ORR, mDoR 3.1 months
- ACR-368 clinical activity (without patient selection) in past platinum-resistant ovarian trials: ~12% ORR, mDoR >5.6 months
  - (BRCA-mutant and BRCA wild type patients regardless # lines of prior therapy; Lilly-sponsored 46-center, 8-country, N=169 patient study)^
- TPP - high grade PROC: ≥25% ORR with CI lower bound >15%
- TPP - high grade endometrial cancer: ≥20-25% ORR with CI lower bound >15%

* Aurelia trial: Pujade-Lauraine E et al, JCO (2014); Corail trial: Gaillard S et al, JCO (2016)
** Ray-Coquard I et al, BJC (2013)
^ Konstantinopoulos P et al, Gyn Oncol. (2022)

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

- RP2D of ACR-368 based on predicted sensitivity using our ACR-368 OncoSignature Assay run by our CDx partner
- 68 sites activated[1]
- Key opinion leaders, some with extensive experience using ACR-368 from previous trials are actively participating



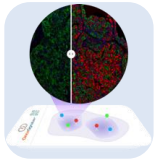
- FDA Fast Track Designation granted May 8, 2023 for ACR-368 monotherapy in OncoSignature-positive patients with Platinum-Resistant Ovarian Cancer and Endometrial Cancer
- FDA Breakthrough Device Designation granted November 16, 2023 for ACR-368 OncoSignature Assay for the identification of ovarian cancer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

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

ACR-368-201 STATUS – OVARIAN AND ENDOMETRIAL (LOCKED ONCOSIGNATURE THRESHOLDS, PROSPECTIVE TRIAL)

OncoSignature-positive
ACR-368 RP2D (105 mg/m^2)

Registrational intent Phase 2

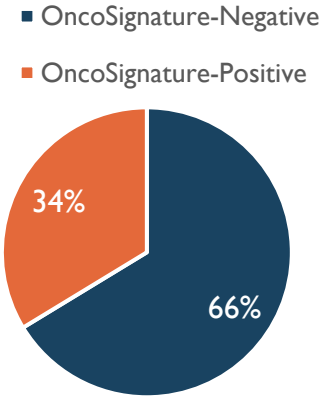


OncoSignature-negative
ACR-368 RP2D (105 mg/m^2) + ULDG RP2D (10 mg/m^2)

Exploratory Phase 1B/2

OncoSignature

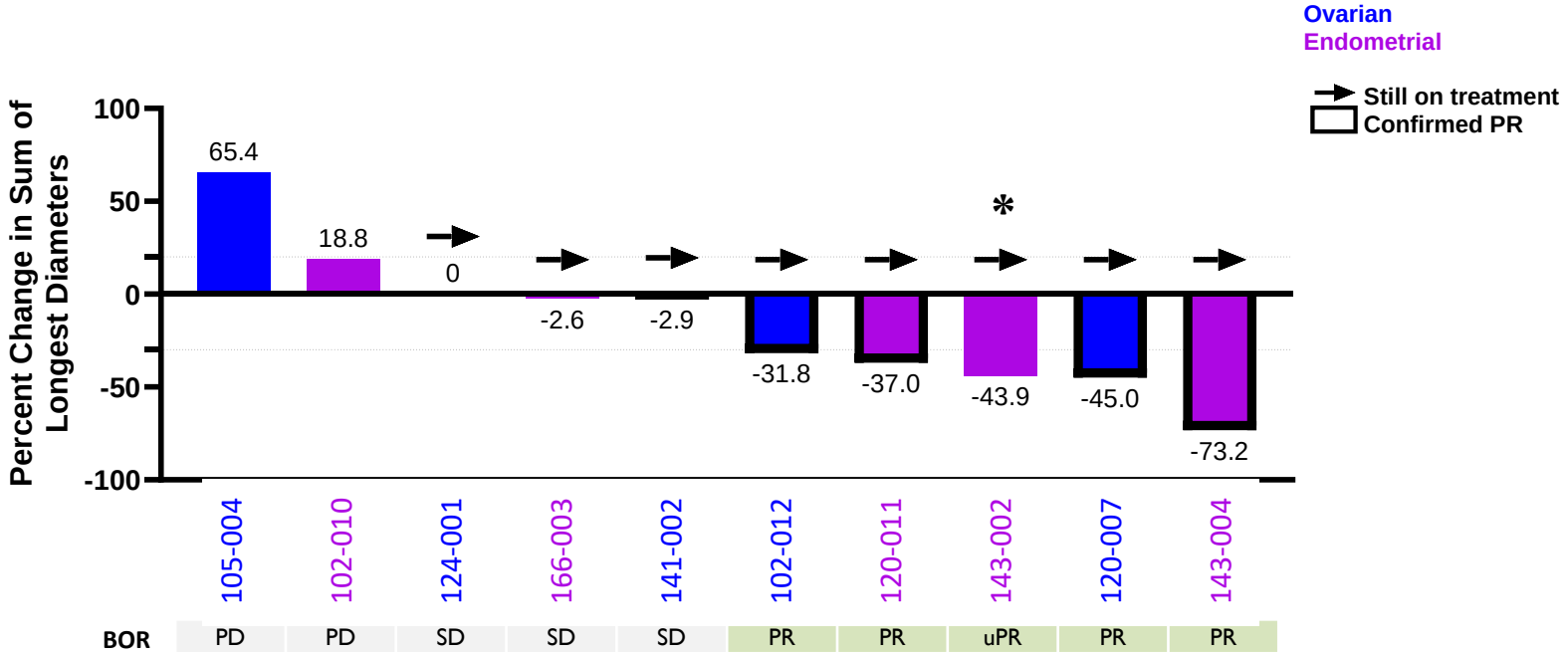
OncoSignature-positive	OncoSignature-negative
Patients enrolled (N = 31)	Patients enrolled (N = 61; incl. 7 to be dosed)
Patients who received at least one dose (N = 26)	Patients who received at least one dose (N = 41)
13 patients awaiting 8-week scan	21 patients awaiting 8-week scan
Patients with at least the 8-wk scan (N = 10)	Patients with at least the 8-wk scan (N = 16)
Patients currently on study (N = 21)	Patients currently on study (N = 28)



OncoSignature-positive rate =34%, consistent with predicted ~35% based on patient tumor sample OncoSignature screening prior to clinical trial

Data cut as of April 1, 2024

ONCOSIGNATURE+ GYN PATIENTS – TUMOR SHRINKAGE
(LOCKED THRESHOLDS, PROSPECTIVE EVALUATION PER PROTOCOL)



*Since data cut off, the one unconfirmed PR has been confirmed bringing the total confirmed PRs to 5

BOR = Best overall response

Data cut as of April 1, 2024

ONCOSIGNATURE-POSITIVE PHASE 2 MONOTHERAPY GYN SUMMARY– PROSPECTIVE DATA WITH LOCKED THRESHOLDS

		Ovarian	Endometrial	Total
OncoSignature Positive (Arm 1)	PR (confirmed)	2	3	5
	SD	2	1	3
	PD	1	1	2
	Total	5	5	10
	ORR	40%	60%	50%

-Ovarian: The 95% CI^ for ORR = (12%, 77%). For reference, ovarian SOC ~12%.

-Endometrial: The 95% CI^ for ORR = (23%, 88%). For reference, endometrial SOC ~ 9%

All 5 confirmed responders on treatment; median DoR not reached

^ Agresti-Coull

Data cut as of April 1, 2024

ACR-368 ONCOSIGNATURE PROSPECTIVELY PREDICTS SENSITIVITY TO MONOTHERAPY IN ONGOING PHASE 2 TRIAL

ORR	BM+ (ARM 1) ACR-368 monotherapy	BM- (ARM 2) ACR-368 + ULDG	Patients (N)
Ovarian	40% (2/5)	0% (0/11)	16
Endometrial	60% (3/5)	0% (0/5)	10
Combined	50% (5/10)	0% (0/16)	26

P value (confirmed PRs) = 0.0038

Notes:

- (non-parametric bootstrap simulation and Fisher test BM+ vs BM-)
- ORR in ovarian all-comer = 12.5%, which is consistent with JTJN study (12%)

Data cut as of April 1, 2024

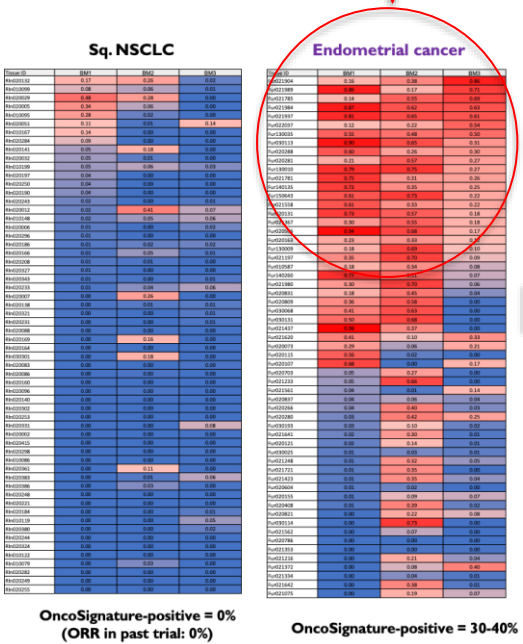
ENDOMETRIAL CANCER IS AN AP3-PREDICTED TUMOR TYPE

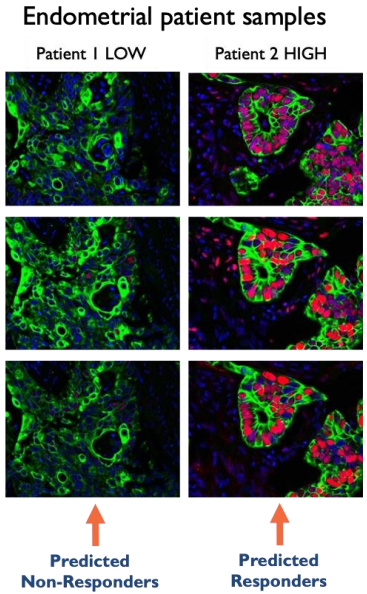
ACR-368 OncoSignature-based indication finding prior to trial entry

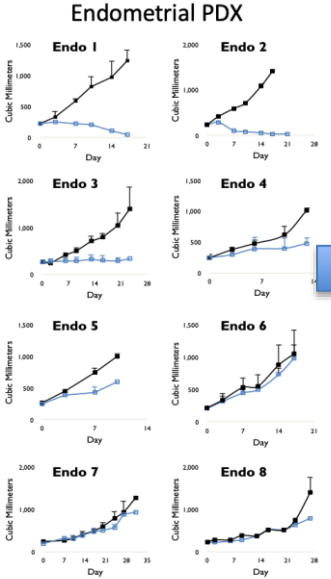
ACR-368 OncoSignature imaging demonstrates addiction to CHK1/2 DDR axis

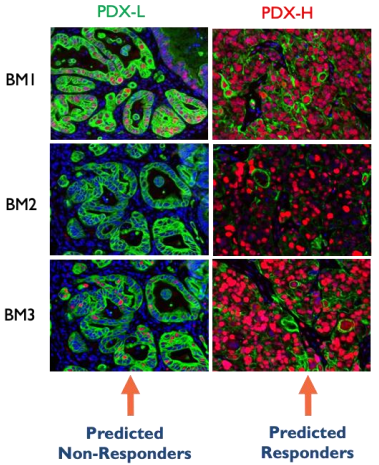
Confirmation of predicted sensitivity in genetically non-modified PDX models

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







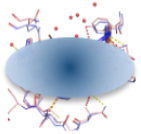


in >1,000 cancer patients treated with ACR-368 in Lilly-sponsored trials, endometrial cancer was not tested

INTERNAL PIPELINE: ADVANCING DEVELOPMENT CANDIDATE ACR-2316 AND OTHER PROGRAMS - LEVERAGING AP3

ACR-2316 and DDR programs

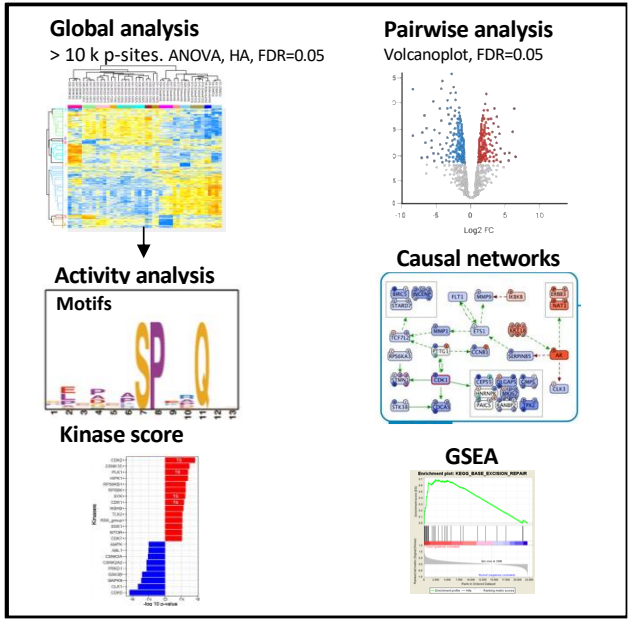
- >40 high resolution co-crystals (1.5-3.1 Å) and novel WEE1- and PKMYT1-selective structural series and lead candidates
- ACR-2316 a novel, potent, selective dual inhibitor
- Designed by AP3 to overcome WEE1 and PKMYT1 single inhibitor resistance
- IND target date Q3 2024 and trial initiation Q4 2024



Cell cycle inhibitor program with undisclosed target

- Anticipated development candidate 2025

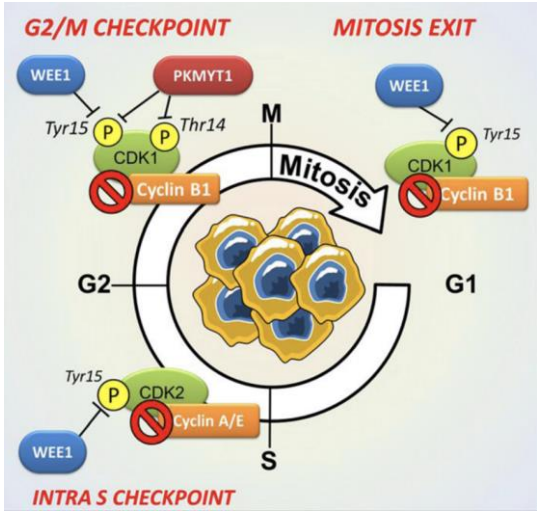
High throughput AP3 profiling



AP3 used for biologically relevant selectivity profiling

WEE1 AND PKMYT1 ARE ATTRACTIVE CANCER TARGETS: IDEAL FOR AP3 APPROACH

- 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



Ghelli Luserna di Rorà et al. J. Hematol Oncol, 2020

- 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

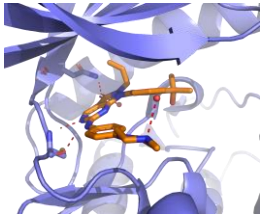
Program goals:

- **Superior single agent activity (AP3)**
  - AP3-guided design to overcome WEE1 and PKMYT1 single inhibitor resistance through balanced dual inhibition
- **High selectivity and potency (co-crystallography)**
  - Structure-guided design to limit adverse events (AEs) to be on-target, transient, mechanism-based
- **Streamlined clinical development (ACR-2316 OncoSignature)**
  - To identify/prioritize sensitive indications prior to clinical start and for drug target engagement-based dose optimization

ACR-2316: Rationally designed WEE1/PKMYT1 development candidate

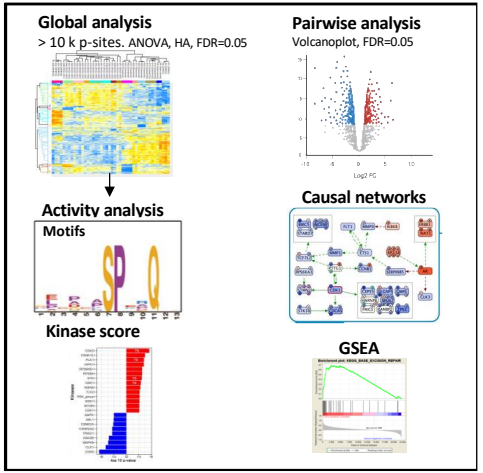
- ✓ 5-20-fold more potent in preclinical models than clinical benchmarks
- ✓ Superior anti-tumor efficacy with complete tumor regression across models
- ✓ High selectivity ensures transient, short-lived, mild AEs
- ✓ Potent WEE1 inhibition, balanced PKMYT1 inhibition, overcomes resistance

Co-crystallography for drug design and selectivity



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

AP3 used for biologically optimal SAR



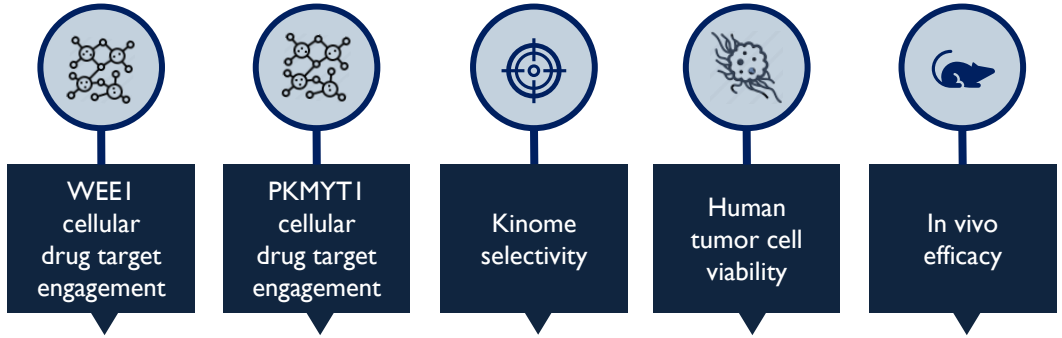
ACR-2316 IS A POTENTIALLY BEST-IN-CLASS AGENT RATIONALLY DESIGNED USING ACRIVON'S AP3 PLATFORM

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

AP3-Enabled SAR

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

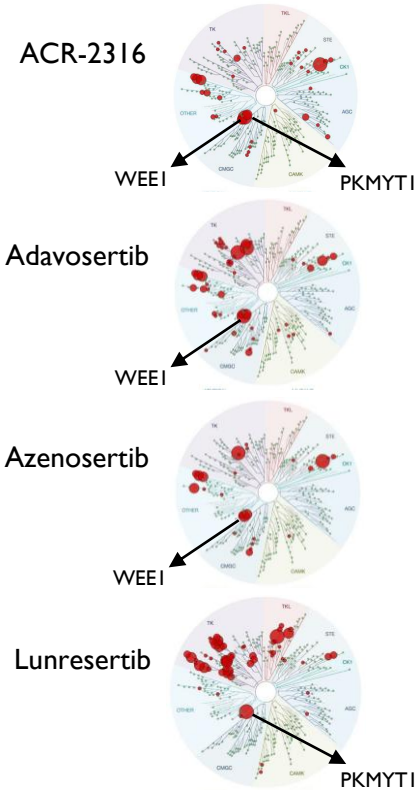
ACR-2316 SHOWS ATTRACTIVE PROFILE IN ONGOING PRECLINICAL STUDIES



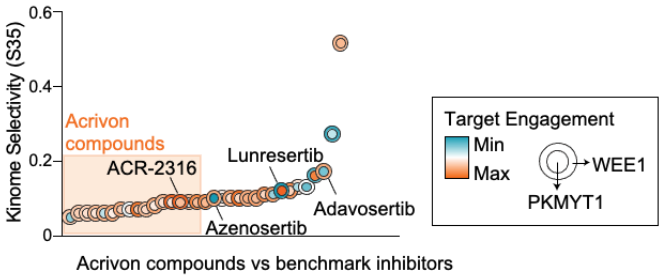
Relative performance					
ACR-2316	**++++**	**++**	**++++**	**++++**	**++++**
Adavosertib	++	-	++	+++	++
Azenosertib	++	-	+++	++	++
Debio0123	+	-	++++	+	+
Lunresertib	-	+++	+	+	+

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

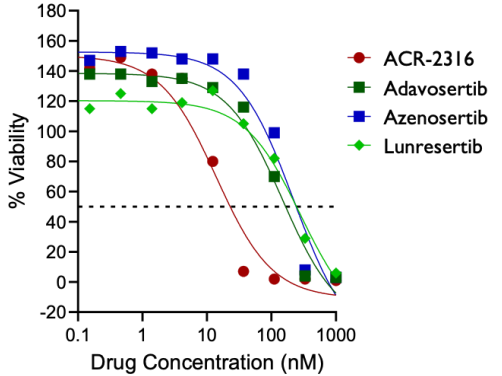
KinomeScan (468 kinases @ 1μM)



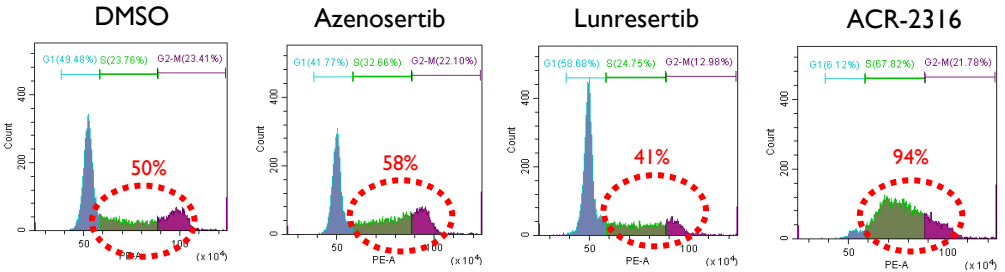
ACR-2316 is highly selective (KinomeScan)



ACR-2316 potently inhibits cancer cell viability



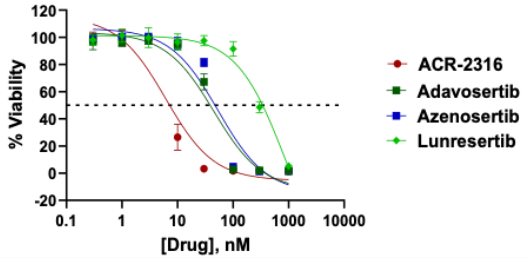
ACR-2316 exerts potent cell cycle effects with pronounced S-G2/M accumulation



100 nM, 24 hour

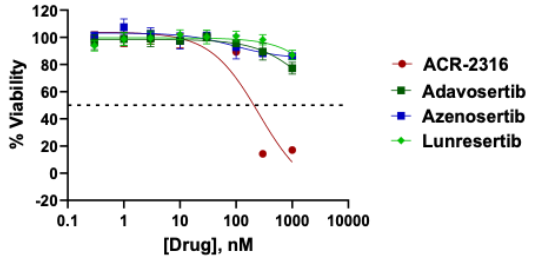
ACR-2316 SHOWS SUPERIOR ACTIVITY VS BENCHMARKS ACROSS ALL HUMAN TUMOR CELL LINES TESTED

Human Tumor Cell Line 1



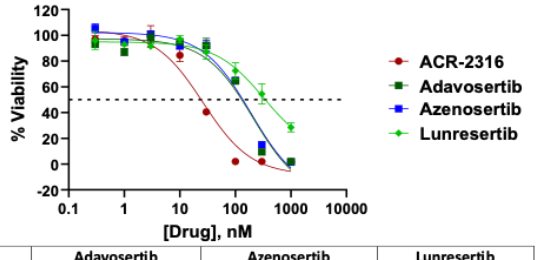
ACR-2316 IC50 (nM)	Adavosertib IC50 (nM)	Azenosertib IC50 (nM)	Lunresertib IC50 (nM)
7	39	47	340

Human Tumor Cell Line 2



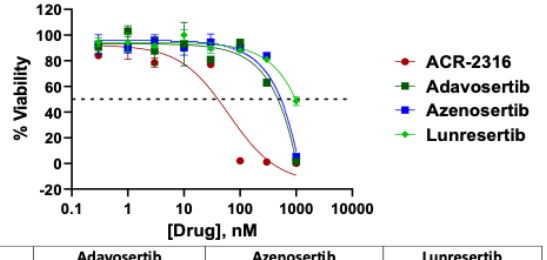
ACR-2316 IC50 (nM)	Adavosertib IC50 (nM)	Azenosertib IC50 (nM)	Lunresertib IC50 (nM)
207	> 1000	> 1000	> 1000

Human Tumor Cell Line 3



ACR-2316 IC50 (nM)	Adavosertib IC50 (nM)	Azenosertib IC50 (nM)	Lunresertib IC50 (nM)
24	130	136	345

Human Tumor Cell Line 4



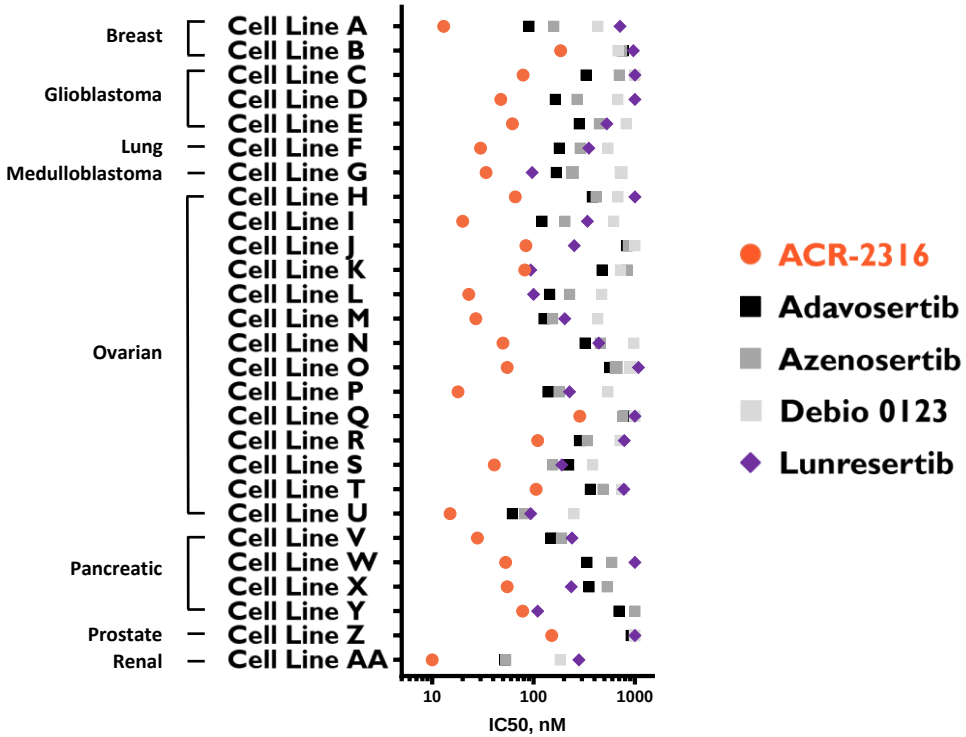
ACR-2316 IC50 (nM)	Adavosertib IC50 (nM)	Azenosertib IC50 (nM)	Lunresertib IC50 (nM)
40	471	533	967

Example: Ovarian human cancer cell lines

19 ovarian and other human tumor cell lines tested to date

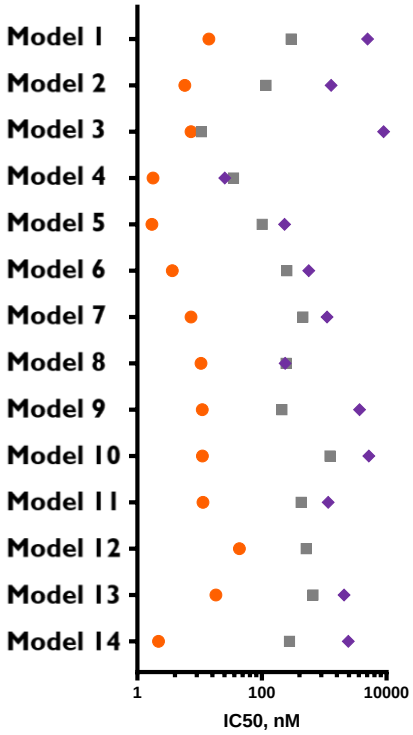
ACR-2316 IS HIGHLY POTENT ACROSS HUMAN TUMOR CELL LINES AND PATIENT-DERIVED *EX VIVO* TUMOR MODELS

Human tumor cell lines



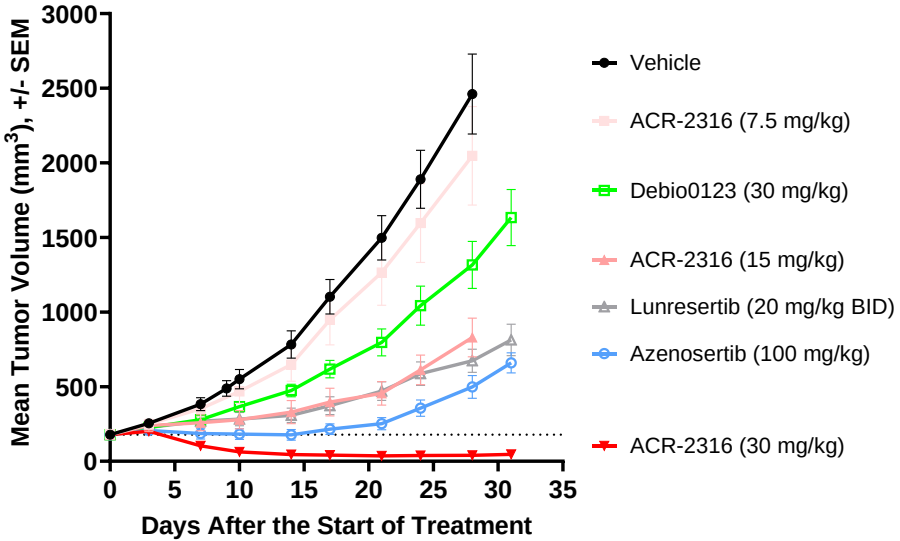
ACR-2316
Adavosertib
Azenosertib
Debio 0123
Lunresertib

Patient-derived *ex vivo* tumor models

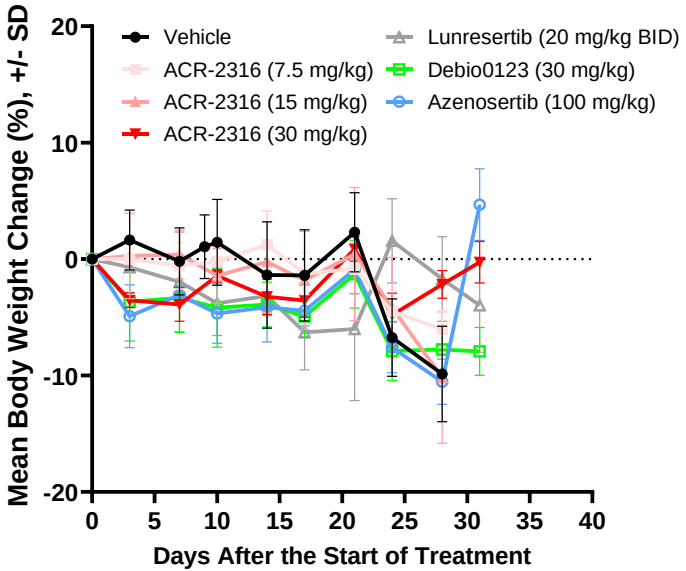


ACR-2316 SHOWS POTENT ANTI-TUMOR ACTIVITY COMPARED TO CLINICAL WEE1 OR PKMYT1 INHIBITORS – MODEL 1

Efficacy (5d on/2d off)

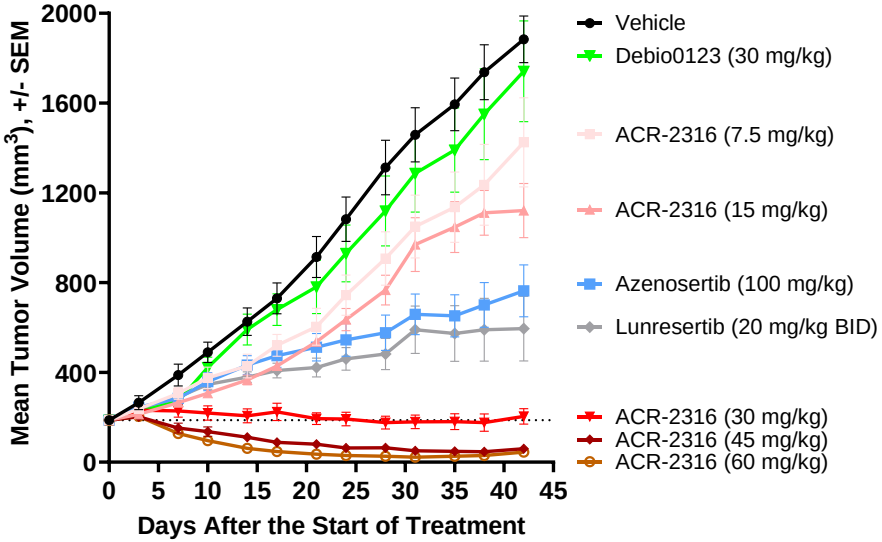


Tolerability (5d on/2d off)

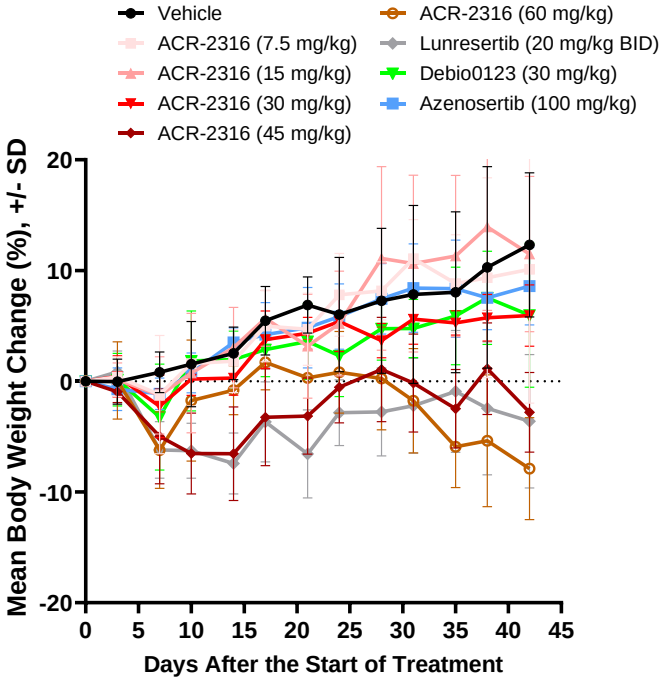


ACR-2316 SHOWS POTENT ANTI-TUMOR ACTIVITY COMPARED TO CLINICAL WEE1 OR PKMYT1 INHIBITORS – MODEL 2

Efficacy (5d on/2d off)

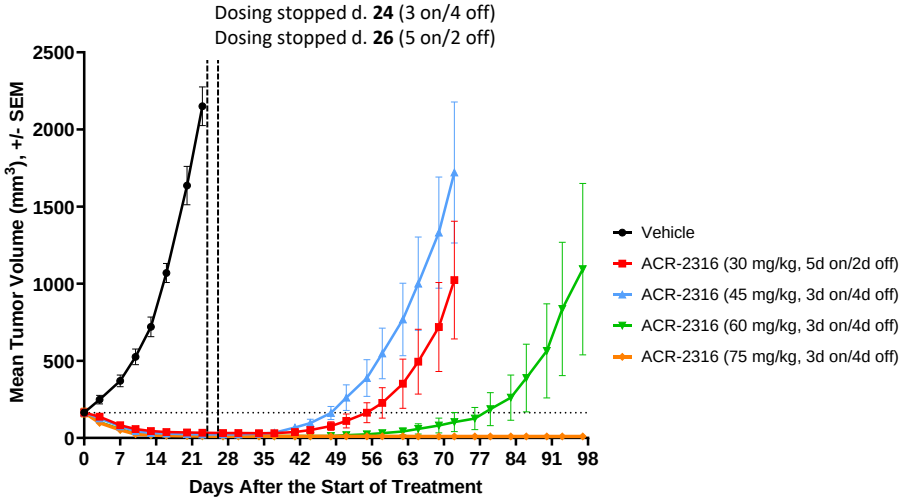


Tolerability (5d on/2d off)

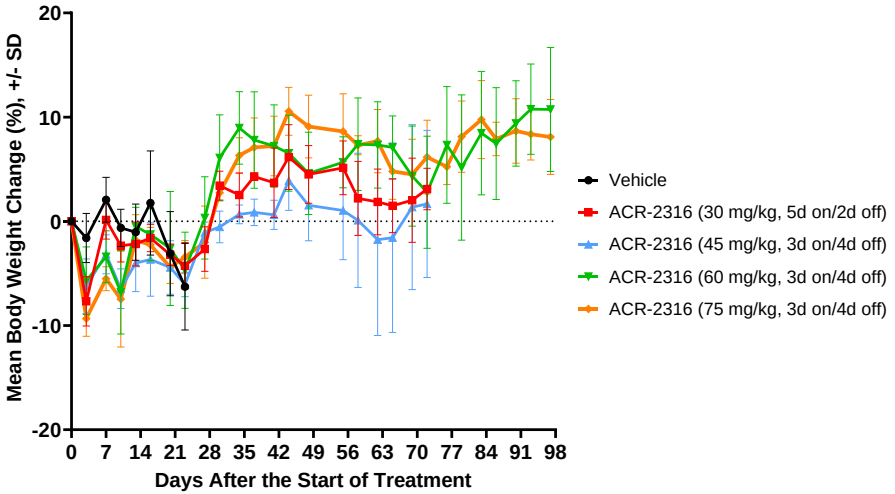


ACR-2316 LEADS TO POTENT AND DURABLE TUMOR REGRESSION

Efficacy

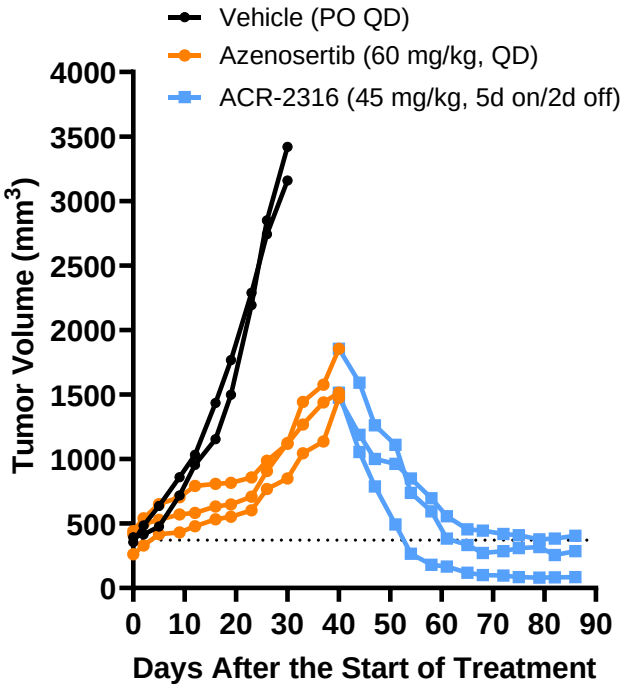


Tolerability

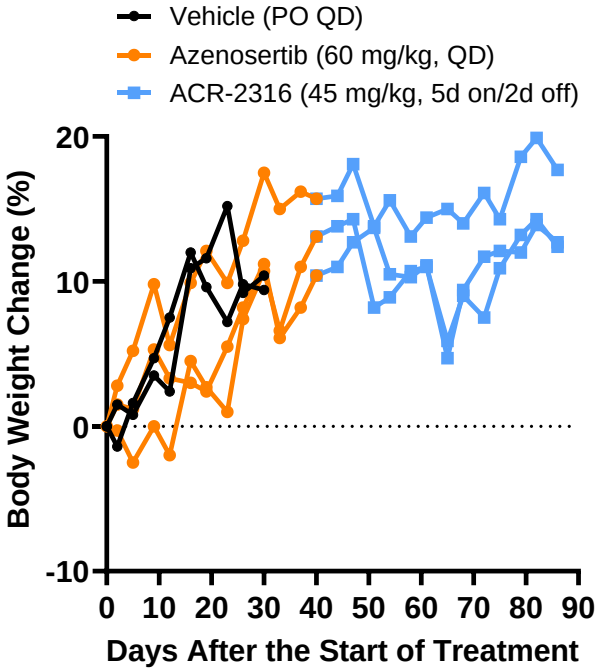


ACR-2316 SHOWS DEEP REGRESSION IN TUMORS PROGRESSING ON A BENCHMARK WEE1 INHIBITOR

Anti-tumor activity

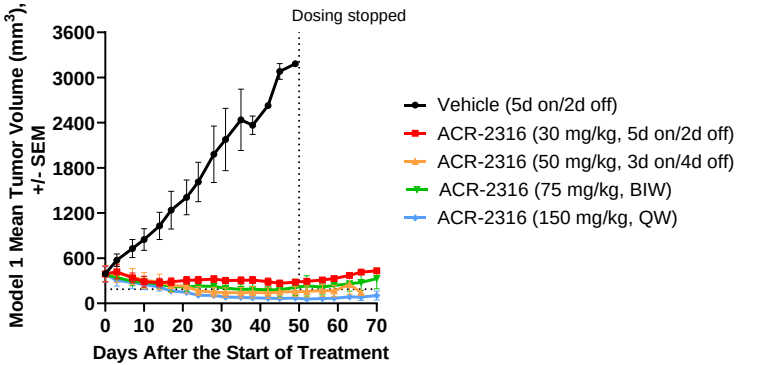


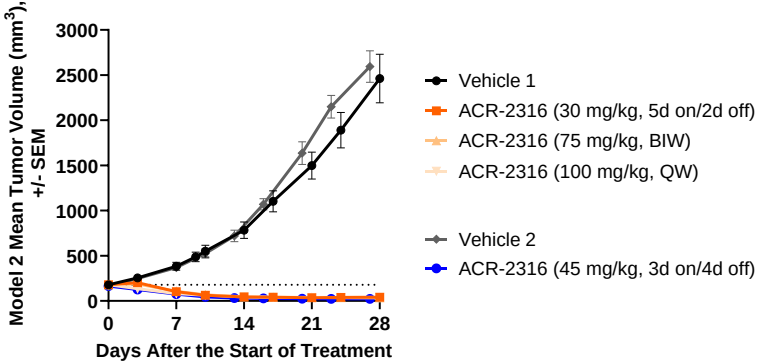
Tolerability



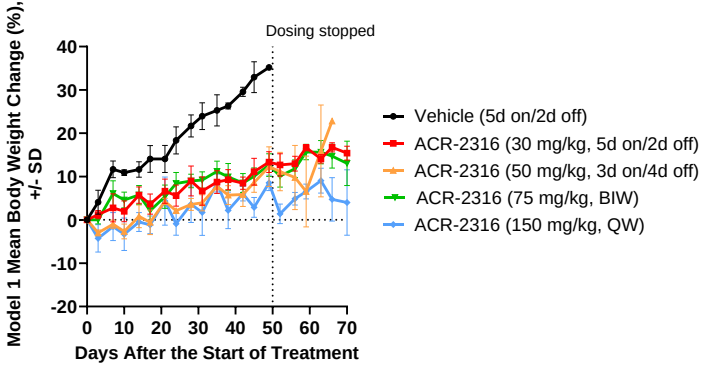
STRONG ACR-2316 EFFICACY DEMONSTRATED ACROSS BROAD RANGE OF DOSING REGIMENS AND MODELS

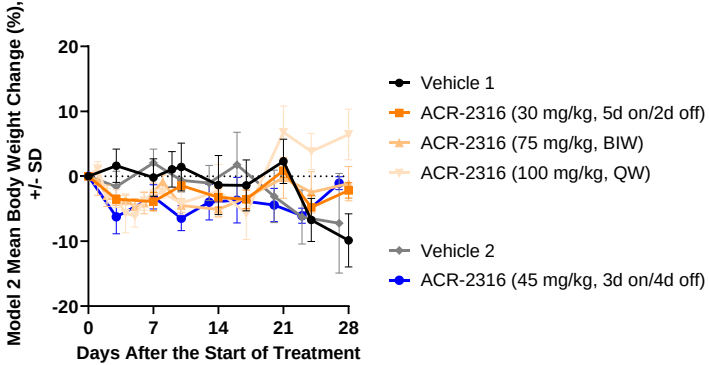
Efficacy



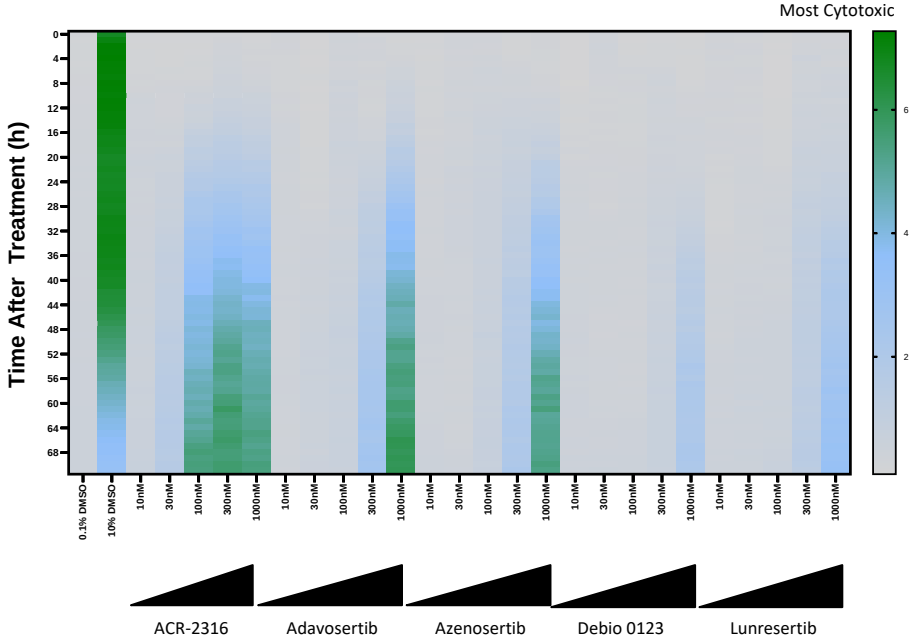


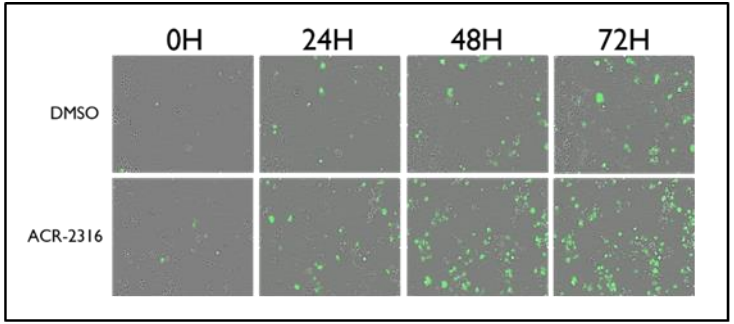
Tolerability





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

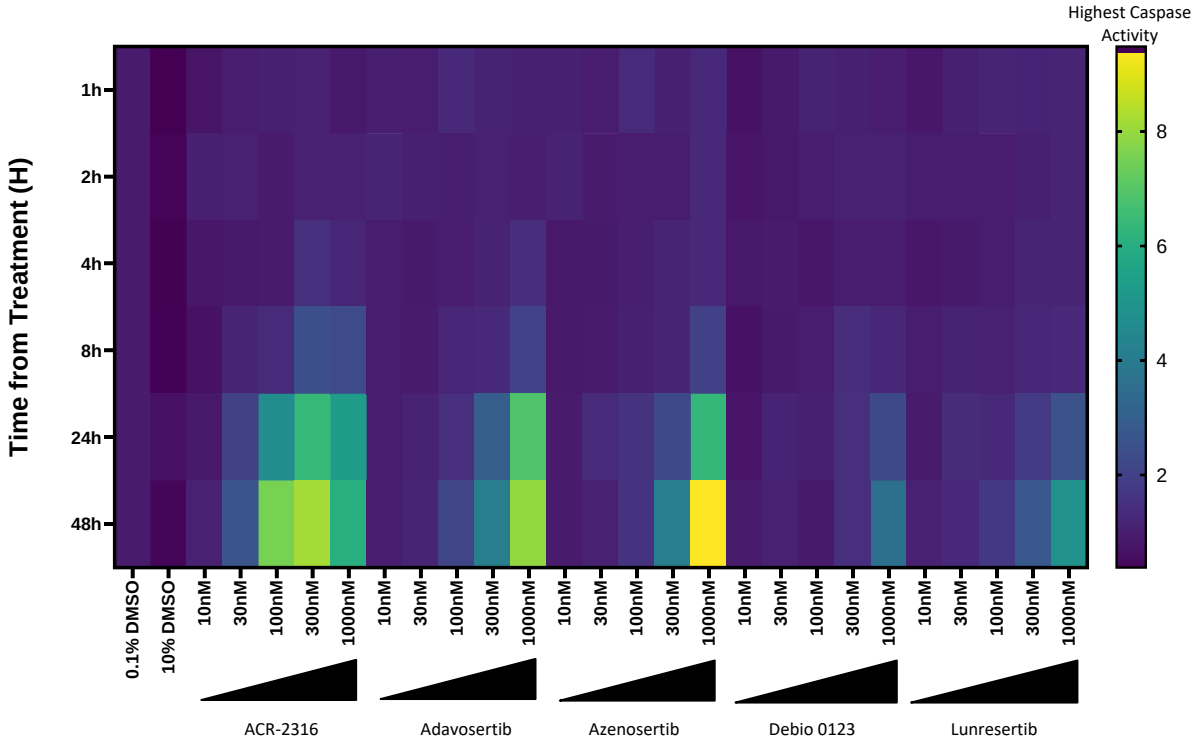




Representative images of OVCAR3 cells treated with 0.1% DMSO or 100 nM ACR-2316 (green fluorescence = dead cells)

CellTox-Green Assay

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



Caspase 3/7-Glo Assay (OVCAR3 Cells)

ACR-2316 - FAVORABLE PRECLINICAL SAFETY PROFILE

Mice:

- ACR-2316 is 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

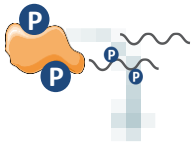
Rat and dog MTD, DRF, and GLP tox studies:

- MTD ≥ 30 mg/kg in both species (single dose)
- GLP tox studies (31 days) completed in rat and dog with the planned human dosing regimen achieving exposure required for tumor regression
- Minimal hematological effects in rats, except for mechanism-based transient, fully reversible reticulocytopenia between dosing cycles
- Mechanism-based, reversible food/GI effect in dogs, not impeding weight gain

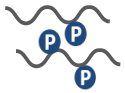
STREAMLINED AP3-BASED BIOLOGICAL SAR OPTIMIZATION FOR SINGLE AGENT ACTIVITY OF PRECLINICAL PROGRAMS

Drug treatment

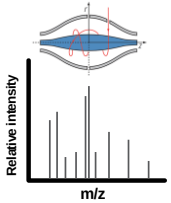
Proteolysis
P-peptide enrichment



Peptide clean up



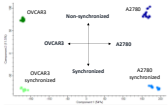
Ultra high resolution
P-proteomic profiling



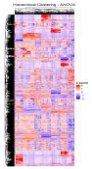
Direct DIA analysis

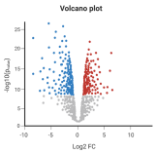
High resolution and throughput MS-based P-proteomics

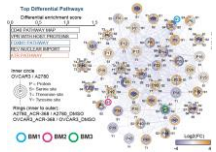
Quantitative mapping (>105,000 phospho-sites covering >10,000 proteins)



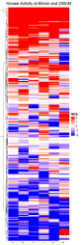
Drug-regulated phospho-sites and biological process enrichment

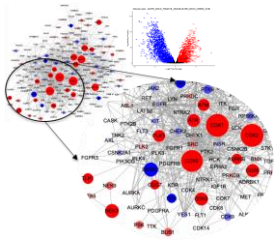


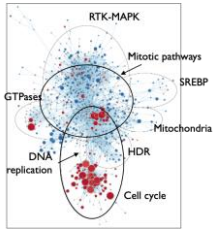




Drug-regulated pathway activity mapping and reconstitution







Proprietary pipe for automated AP3 analyses with actionable results

Week 0

Turnaround <2 weeks

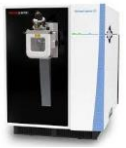
Week 2

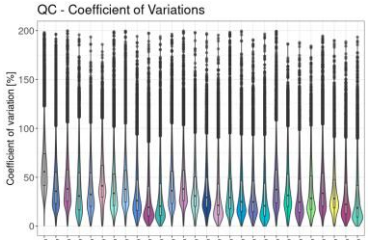
AP3: TIGHT, HIGH-RESOLUTION DATA WITH DEEP COVERAGE

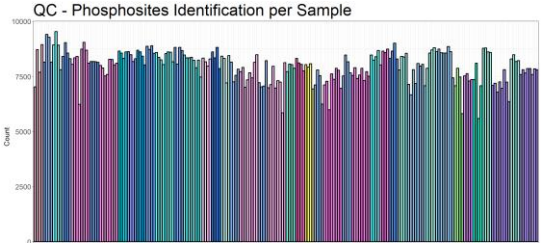
35388 p-sites

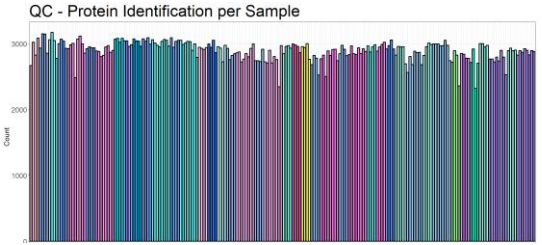
15733 p-sites

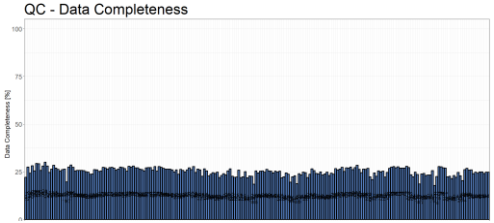
QC MS Data → Data Clean Up → QC Processed Data → Volcano Plots → Hierarchical Clustering → Consensus Sequence Motif → Kinase Inference → Pathway Enrichment → Functional Annotation → Network Mapping → Biomarkers

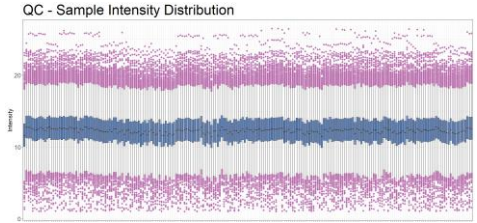


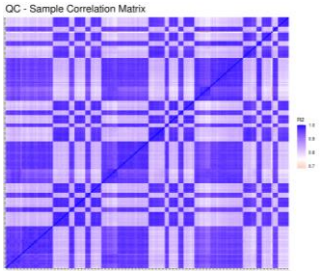






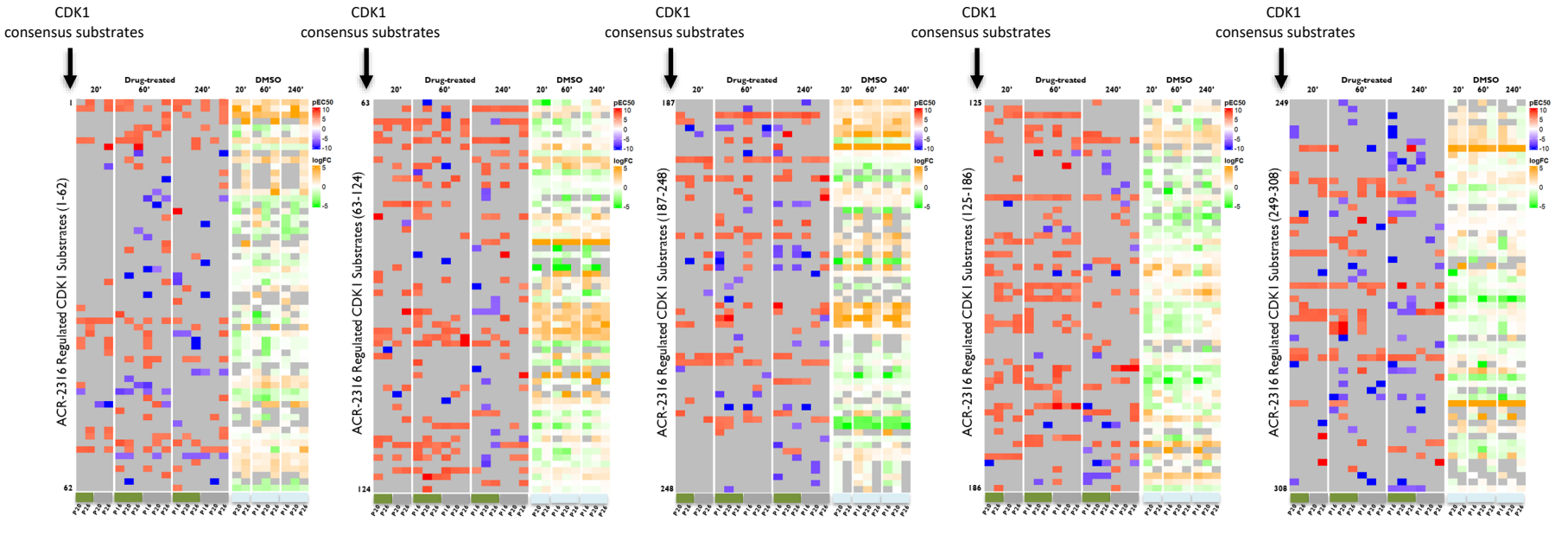






- ✓ Acrivon proprietary compound data (~50 million data points per experiment); dozens of compounds profiled
- ✓ Miniaturized, high throughput, scalable: <2 weeks turn-around, automated AI computational analyses in 1 day
- ✓ Actionable results: Resistance mechanisms, rational combinations, drug-tailored OncoSignature patient selection

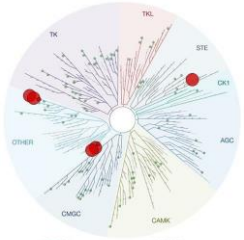
ACR-2316 RESULTS IN STRONG ACTIVATION OF CDK1 ACROSS CELL LINES



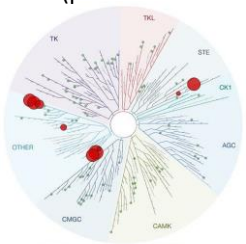
- Unbiased quantitation of ACR-2316-regulated CDK1 substrate p-sites (308) in intact cells based on CDK1 consensus recognition motif (Acrivon proprietary hybrid database approach) across multiple experiments
- Actionable insight into drivers of mitotic catastrophe and on-target CDK1-driven pathways

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

ACR-2316

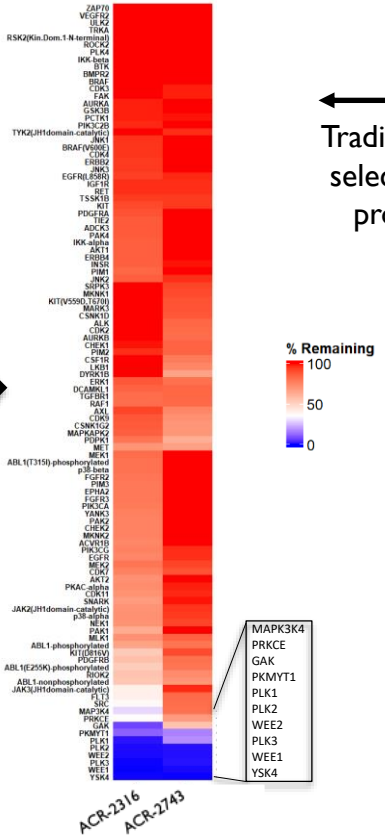


ACR-2743 (previous lead candidate)



Time : 60 minutes
Dose : 20 nM

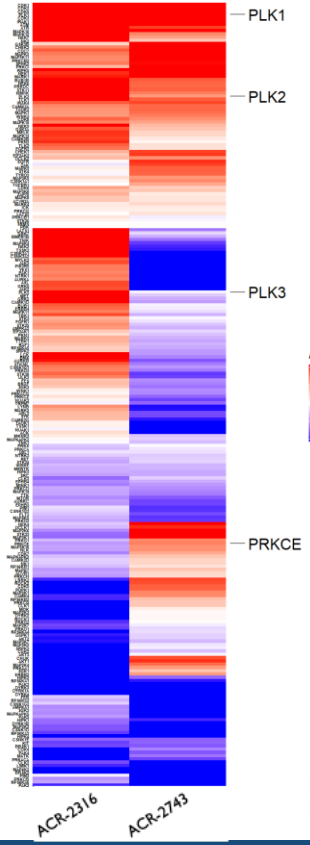
KinomeScan @ 1μM

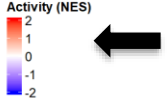


Traditional selectivity profiling

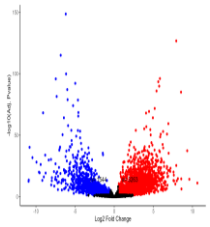
AP3-based pathway profiling

Drug-regulated kinase activity* in intact cells

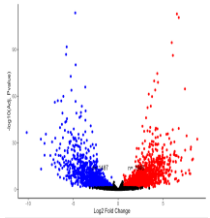




ACR-2316



ACR-2743

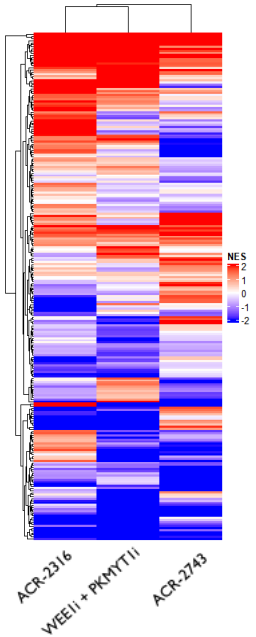


*Kinase activity based on substrate motif analysis using a proprietary PTM-SEA hybrid method

OPTIMIZED DUAL INHIBITORS SHOW DESIRABLE PATHWAY EFFECTS

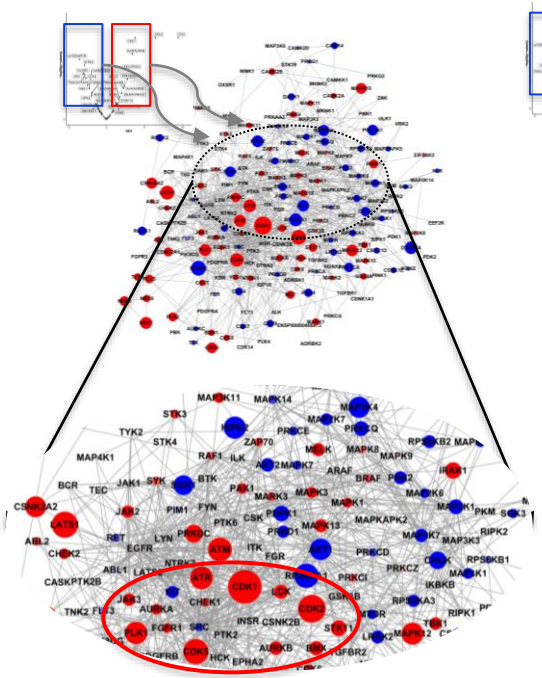
Optimized dual WEE1 and PKMYT1 inhibitors affect cell cycle and canonical MAPK pathways in desirable manner

Substrate motif-inferred kinase activities

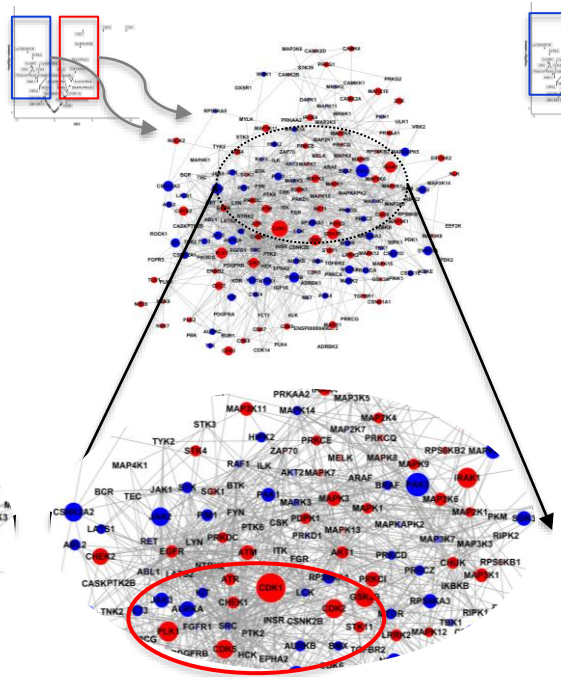


Kinase activity based on proprietary PTM-SEA-based hybrid workflow and analyses

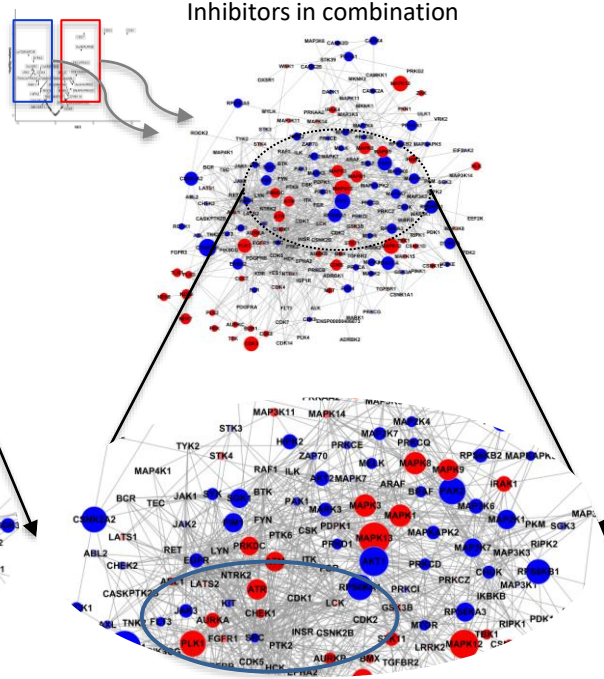
ACR-2316

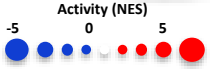


ACR-2743



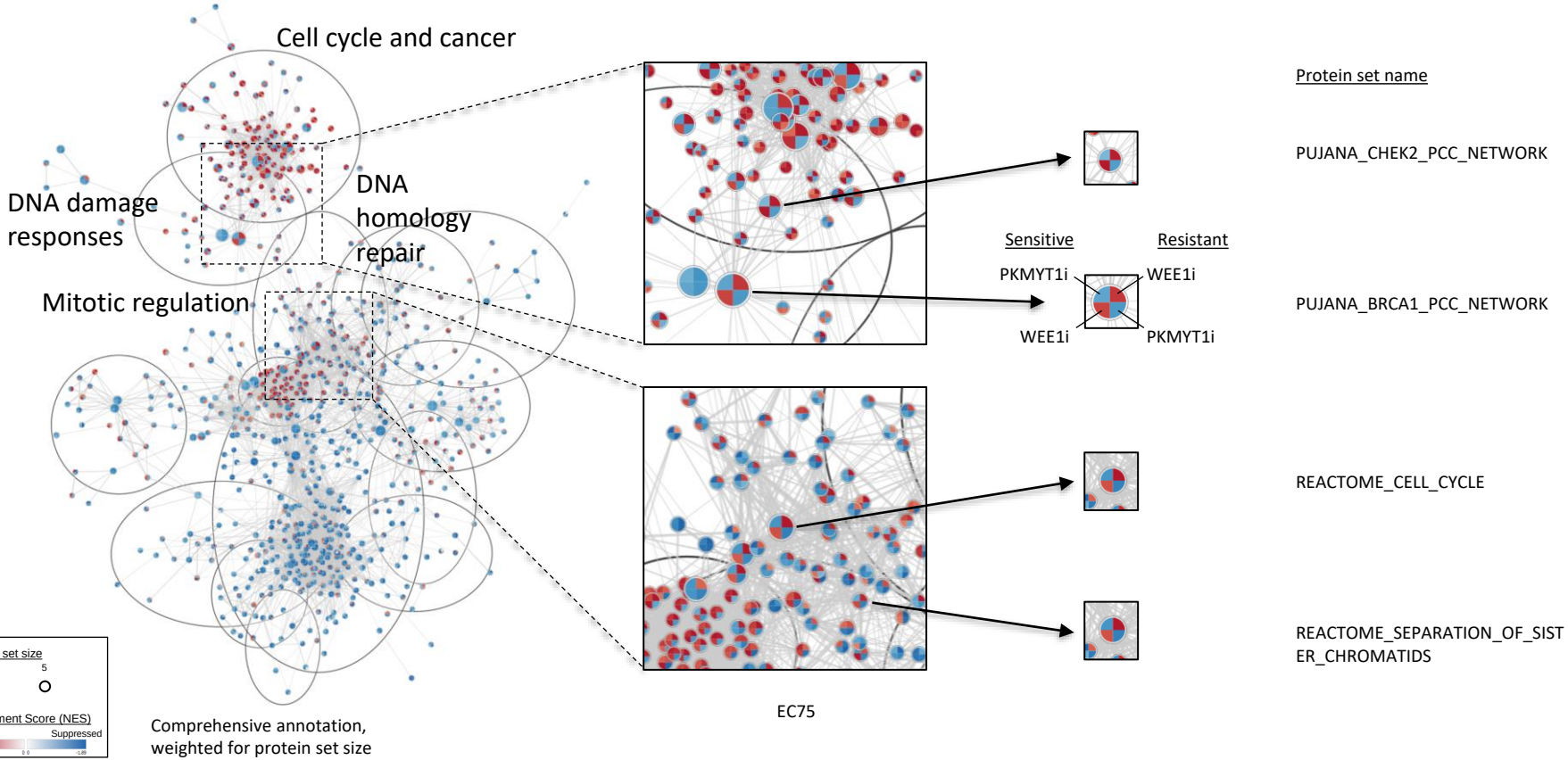
Benchmark* WEE1 + PKMYT1 Inhibitors in combination



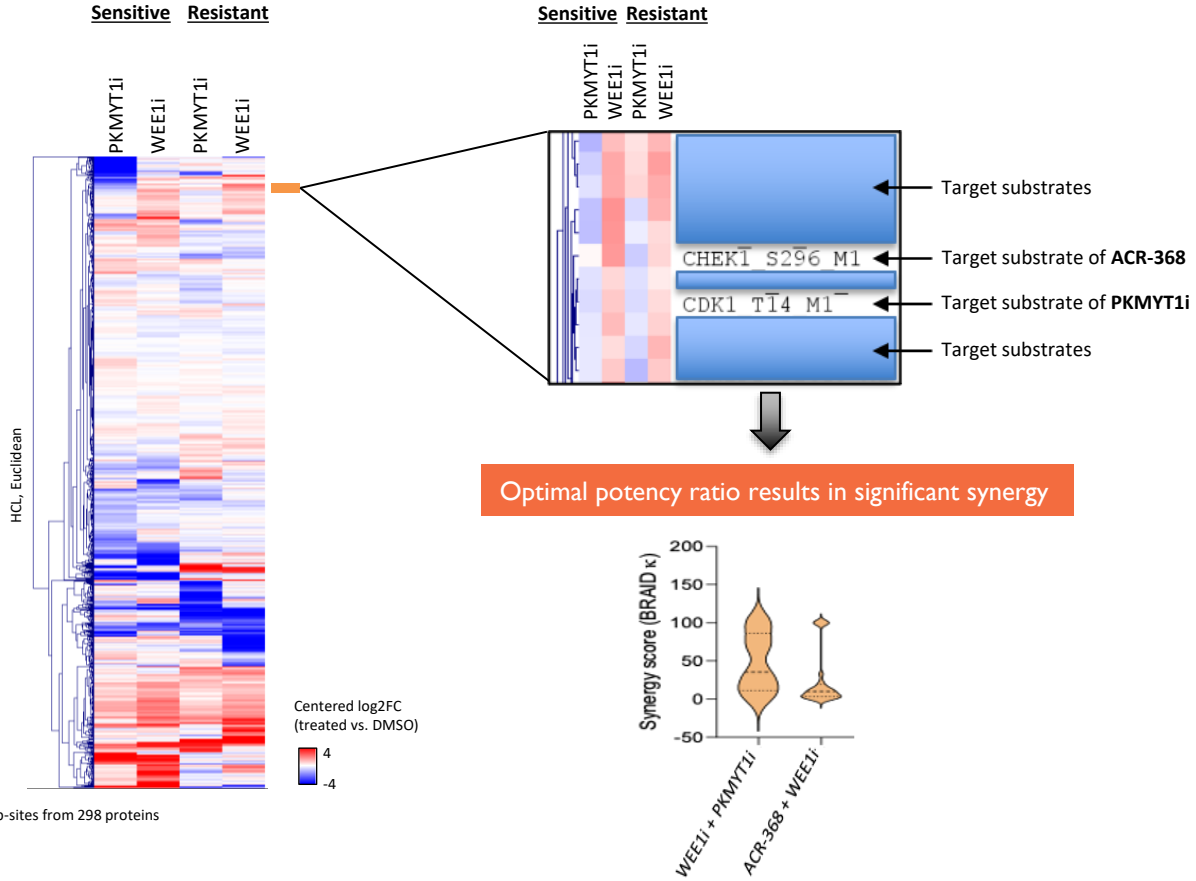


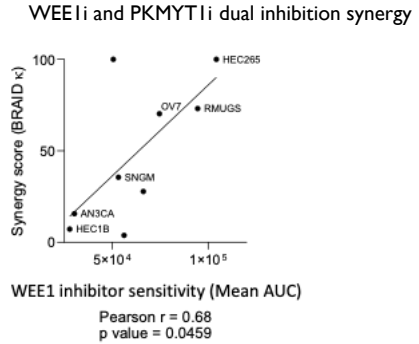
*Clinical-stage selective WEE1 and PKMYT1 inhibitors

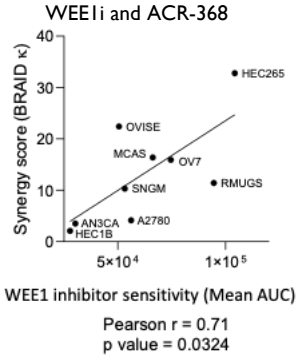
AP3-DERIVED DUAL POTENCY OPTIMIZATION TO OVERCOME WEE1 INHIBITOR RESISTANCE: RECIPROCAL QUENCHING



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







EXPEDITING ACR-2316 TOWARDS CLINICAL MONOTHERAPY DEVELOPMENT

A novel, AP3-enabled, internally discovered dual WEE1 / PKMYT1 inhibitor

Rational Design

- Optimized via AP3
- AP3-enabled design for optimized single agent activity

Superior Profile

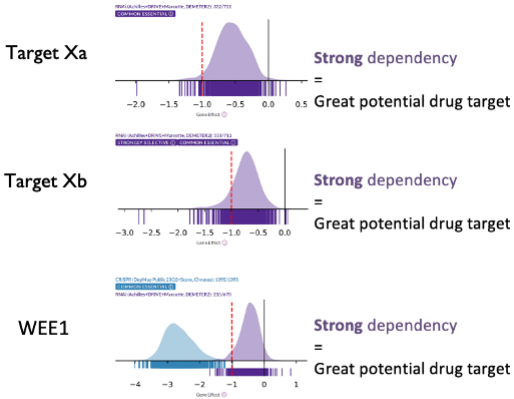
- Potent anti-tumor activity across human tumor cell lines and in tumor-bearing mice vs benchmarks

Streamlined Development

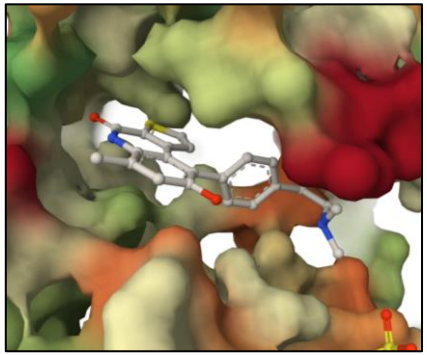
- Rapidly advancing towards IND in Q3 2024, aiming for monotherapy development
- OncoSignature development for indication finding
- Dose optimization to be guided by drug target engagement (BM2)

CELL CYCLE REGULATORY PIPELINE PROGRAM (UNDISCLOSED TARGET)

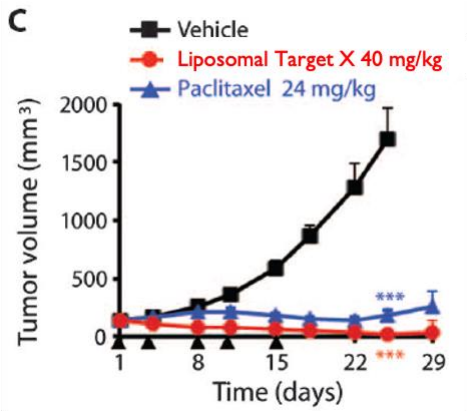
- Target X – an exciting cancer drug target, no/minimal competitor programs, perfectly suited for AP3 platform
- DepMap data suggest suggest target X is an essential gene for cancer cell viability
- Strong mechanistic target rationale for role in oncogenesis
- Highly selective tool compound shows strong 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)

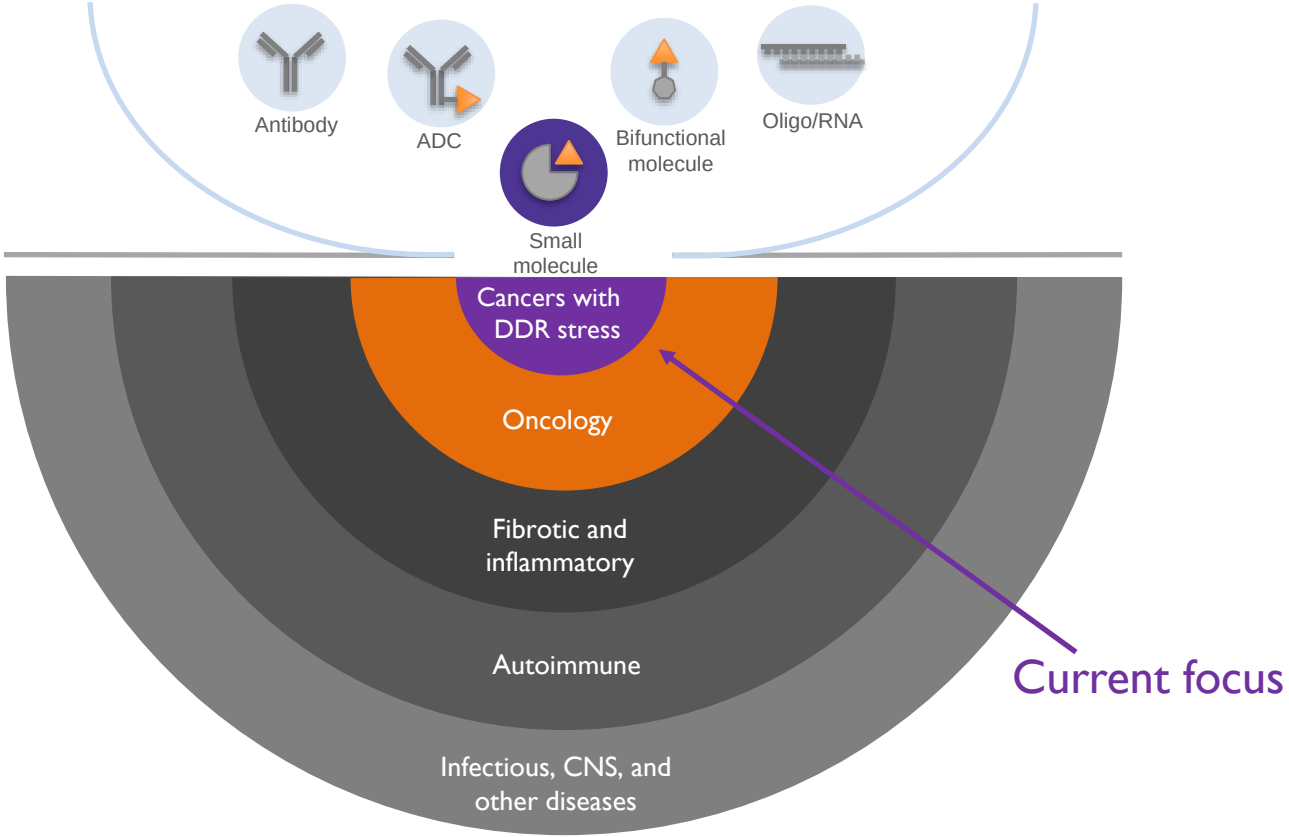


Development candidate 2025

THE AP3 APPROACH IS MODALITY AND DISEASE AGNOSTIC

Therapeutic modalities

Therapeutic areas



FINANCIAL HIGHLIGHTS

Cash and marketable securities

$220.4M

Balance sheet 30-June-2024

Projected runway into

H2'26

Current operating plan, assuming no additional financing

Fully Diluted Shares Outstanding

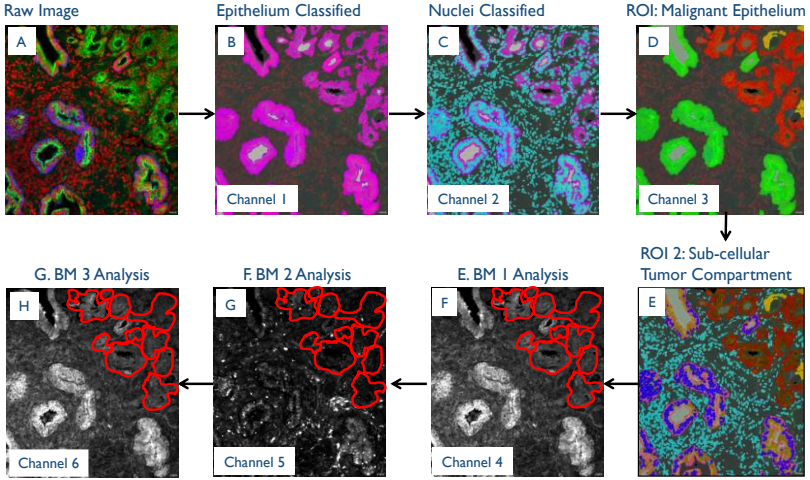
43.9M

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

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

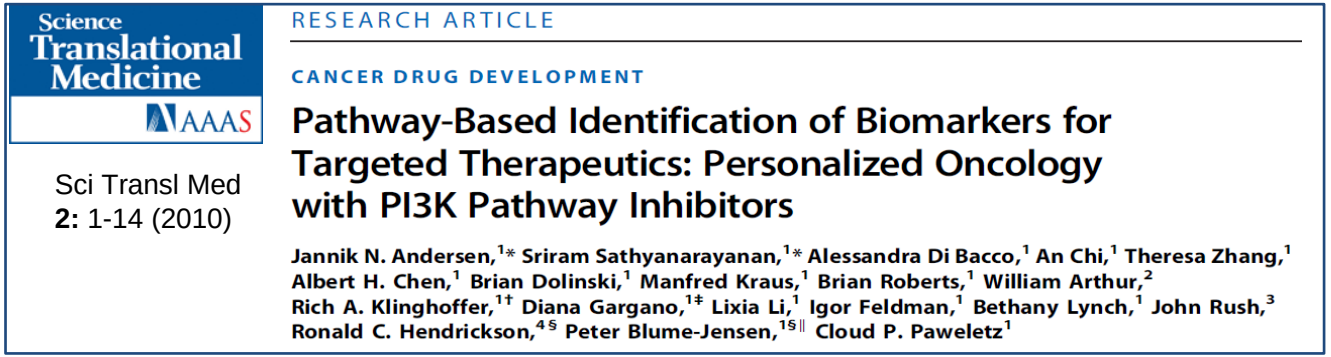
(2015)

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 PI3'K PATHWAY INHIBITOR BIOMARKERS



Science Translational Medicine
AAAS

Sci Transl Med
2: 1-14 (2010)

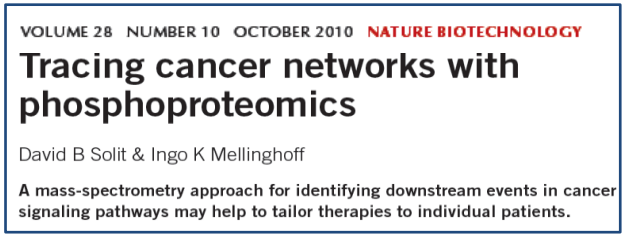
RESEARCH ARTICLE

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:

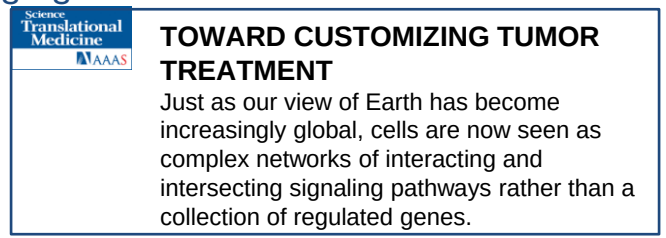


VOLUME 28 NUMBER 10 OCTOBER 2010 NATURE BIOTECHNOLOGY

Tracing cancer networks with phosphoproteomics

David B Solit & Ingo K Mellinghoff

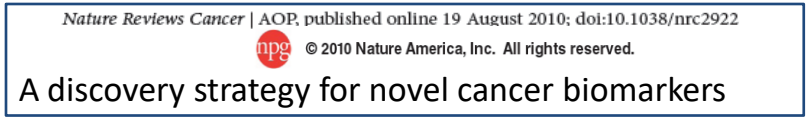
A mass-spectrometry approach for identifying downstream events in cancer signaling pathways may help to tailor therapies to individual patients.



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,[1,5,*] and Jesper V. Olsen[1,5,*]

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,[1,2,5] Jón Otti Sigurðsson,[1,5] Zhenyu Xiao,[3,4] Tanveer Singh Batth,[1] Giulia Francioso,[1] Louise von Stechow,[1] Andres Joaquin Lopez-Contreras,[1] Alfred Cornelis Otto Vertegaal,[2*] and Jesper Velgaard Olsen[1,5,*]

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,[1,6] Katarzyna Kowalczyk,[1] 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[1,5,*]

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,[2] Torben F. Ørntoft,[2] Claus L. Andersen,[2] Michael L. Nielsen,[1] and Jesper V. Olsen[1,5,*]

Cell (2019)

Functional mapping of differential signaling by RPTK mutants

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

Alicia Lundby,[1,5,*] Giulia Francioso,[1] Kristina B. Emdal,[1] Jan C. Refsgaard,[1] Sébastien P. Gnosa,[2] Dorte B. Bekker-Jensen,[1] Anna Secher,[1,4] Svetlana R. Maurya,[1] Indranil Paul,[1] Blanca L. Mendez,[1] Christian D. Kelstrup,[1] Chiara Francavilla,[1] Marie Kveiborg,[3] Guillermo Montoya,[1] Lars J. Jensen,[1] and Jesper V. Olsen[1,5,*]

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/s41467-021-27398-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], Friðrik Lund-Johansen[4,12] & Jesper V. Olsen[1,12]

Nature Communications (2021)

Clinically actionable resistance mechanisms

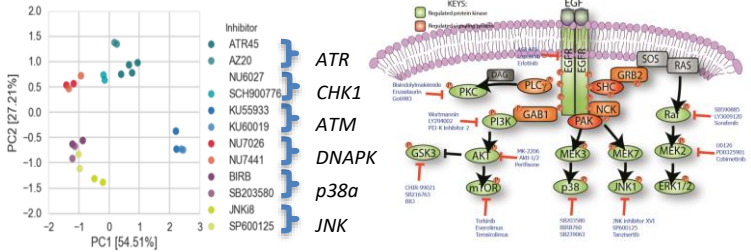
ARTICLE

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 Francioso[1], Jos G. A. Smits[1,2], Sonia Minuzzo[3], Ana Martinez-Val[1], Stefano Indraccolo[3,4] & Jesper V. Olsen[1,12]

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



ADVISORS AND COLLABORATORS

SAB

George Demetri, M.D., FACP, FASCO, FAACR

Professor, Harvard Med. School, Dir. Dana-Farber Cancer Institute & Ludwig Center, Boston

- Leader in Precision Oncology
- Key contributor to development and rapid approvals of Gleevec, Sutent, Stivarga, Zelboraf, Votrient, and Yondelis

Robert Abraham, Ph.D.

EVP, Head Cancer Biology, Odyssey Therapeutics

Adj. Prof. , Burnham Inst.
Adj. Prof. UCSD

- Expert in signal transduction-based R&D
- Previously SVP and WW Head, Oncology R&D, Pfizer
- VP, Oncology Res., Wyeth
- Professor, Burnham Institute
- Professor, Duke University

Timothy Yap, M.B.B.S., Ph.D., F.R.C.P.

Associate Prof., MD Anderson Cancer Center, Medical Director, Inst. for Applied Cancer Science

- Expert on DDR accelerated clinical development and predictive biomarkers
- Previously oncologist Royal Marsden, London and Inst. Cancer Res, London
- Lead/P.I. on numerous DDR trials

David Berman, M.D., Ph.D.

Professor, Director, Queen's Cancer Res. Inst., Ontario Canada

- GU Pathologist; bladder cancer expert
- Expert on protein biomarkers and quantitative tissue imaging
- Academic lead on ProMark®

Jesper V. Olsen, Ph.D.

Academic Co-Founder

Professor, Novo-Nordisk Foundation Protein Center, Cph. University

- Recognized pioneer and leading authority in phosphoproteomics and proteomic systems analyses
- Top 0.1% most cited scientist in protein sciences

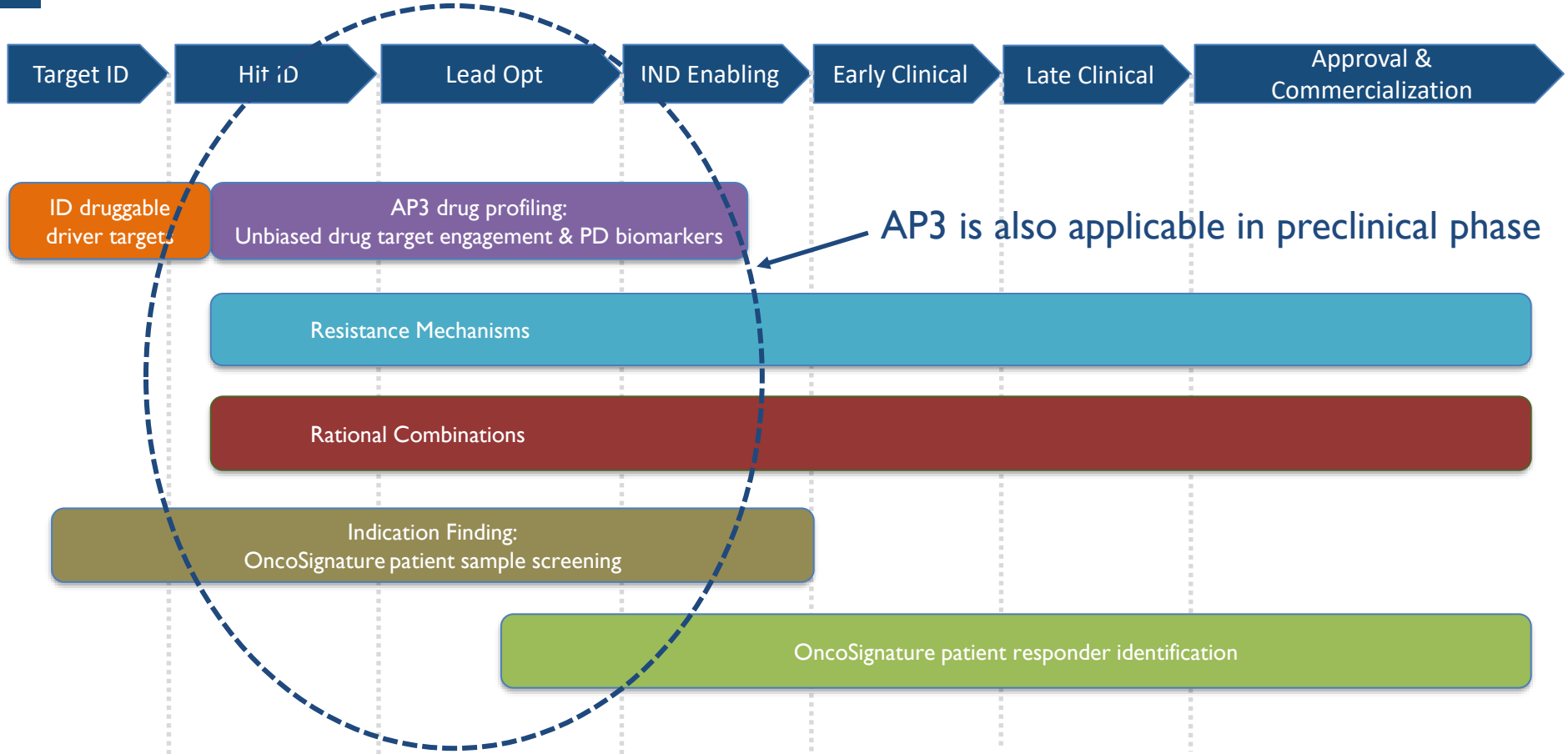
Jung-Min Lee, M.D.

NCI Collaborator

Investigator, Lasker Clinical Research Scholar, NCI

- Expert on women's cancers and DNA damage response (DDR)
- Lead and co-PI on numerous HGSOC &TNBC trials
- Lead PI on ACR-368 platinum-resistant ovarian trials

AP3 IS APPLICABLE ACROSS DRUG DEVELOPMENT STAGES



ACR-2316 MEETS PRE-SPECIFIED DEVELOPMENT CANDIDATE CRITERIA

	Target	ACR-2316
MOA	• AP3 phosphoproteomics-based, optimized MOA; selective, dual WEE1/PKMYT1 inhibition	✓
Potency	• In vitro kinase activity, $IC_{50} \leq 10$ nM • Potent *in cell* target engagement in optimized ratio • Activity across sensitive human tumor cell lines, $IC_{50} < 20$ nM	✓ ✓ ✓
Selectivity	• Kinase panel profiling – highly selective (kinome selectivity) • AP3 profiling confirms desirable CDK and PLK activation for mitotic catastrophe/apoptosis	✓ ✓
ADME/PK	• Orally bioavailable • T½ suitable for once/day dosing	✓ ✓
In vitro safety	• Low in vitro hERG (>10 μM) and CYP inhibition and induction (>1 μM)	✓
Solubility	• > 50 μM for active compounds	✓
PPB	• < 90%	✓
In vivo efficacy	• Demonstrated potent target engagement intratumorally in vivo • Potent single agent activity in CDX models	✓ ✓

KEY DATA: ACR-2316 VERSUS BENCHMARKS

	Assay	ACR-2316	Adavosertib	Azenosertib	Debio123	Lunresertib
Biochemical	Wee1 Binding IC_{50}	1 nM	1 nM	2 nM	1 nM	31 nM
	PKMYT1 Binding IC_{50}	27 nM	155 nM	337 nM	2 µM	10 nM
Cellular Target Engagement	WEE1 EC_{50} (Y15)	2 nM	19 nM	16 nM	109 nM	>10 µM
	PKMYT1 EC_{50} (T14 AlphaLISA)	145 nM	4 µM	2 µM	>10 µM	11 nM
In Vitro Cancer Cell Viability	Human cancer cell viability IC_{50}	11 nM (cell line 1) 17 nM (cell line 2) 21 nM (cell line 3)	52 nM (cell line 1) 127 nM (cell line 2) 96 nM (cell line 3)	48 nM (cell line 1) 111 nM (cell line 2) 128 nM (cell line 3)	165 nM (cell line 1) 338 nM (cell line 2) 94 nM (cell line 3)	372 nM (cell line 1) 400 nM (cell line 2) 173 nM (cell line 3)
	Human PDX (CTG-3226) viability IC_{50}	0.011 µM	N/A	0.209 µM	N/A	3.69 µM
Selectivity	Kinome selectivity: S(35) / S(10)	0.091 / 0.071	0.172 / 0.101	0.101 / 0.071	0.062 / 0.03	0.121 / 0.101
In Vivo Efficacy	CDX model 1 efficacy [T/C (%) / dose mg/kg (frequency)]	0.6 % / 45 mg/kg (QD)	23 % / 60 mg/kg (QD)	26.8 % / 100 mg/kg (QD)	66.4 % / 30 mg/kg (QD)	33 % / 20 mg/kg (BID)
	CDX model 2 efficacy [T/C (%) / dose mg/kg (frequency)]	1.7 % / 60 mg/kg (QD)	N/A	41 % / 100 mg/kg (QD)	87 % / 30 mg/kg (QD)	36 % / 20 mg/kg (BID)
	Ovarian PDX model Efficacy [T/C (%) / dose mg/kg (frequency)]	20 % / 45 mg/kg (QD)	N/A	116 % / 60 mg/kg (QD)	N/A	122 % / 18 mg/kg (BID)

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

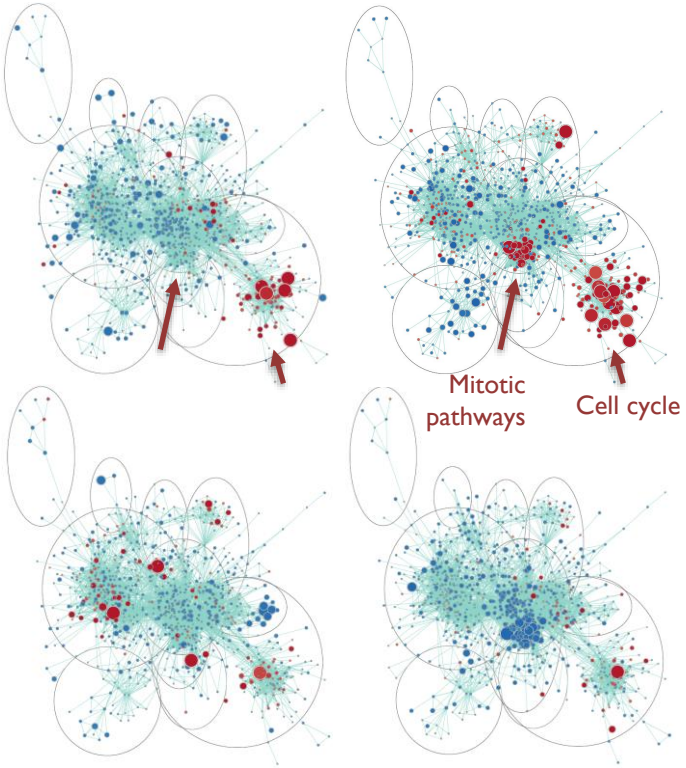
60min
200nM

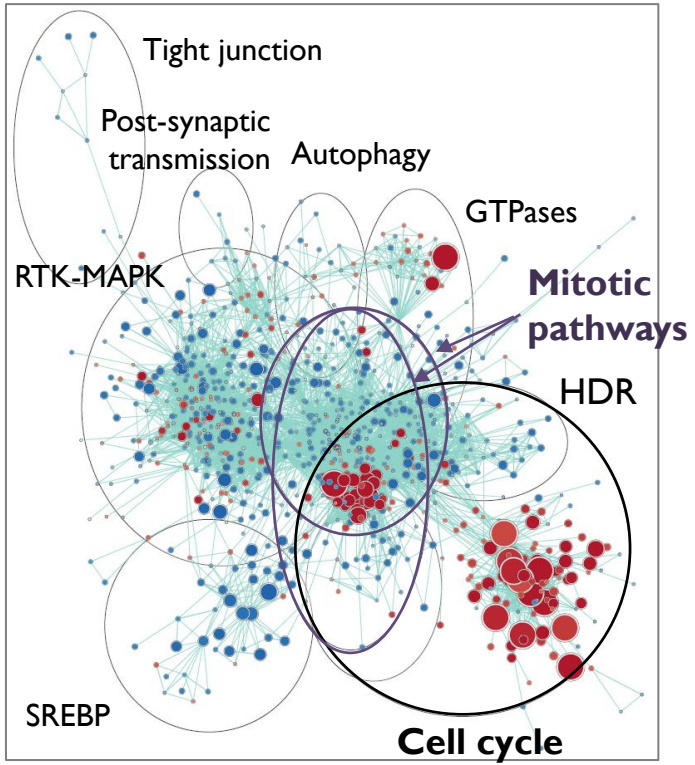
WEE1 inhibitor

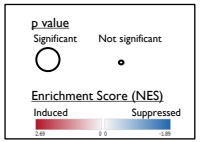
ACR-2316

Sensitive

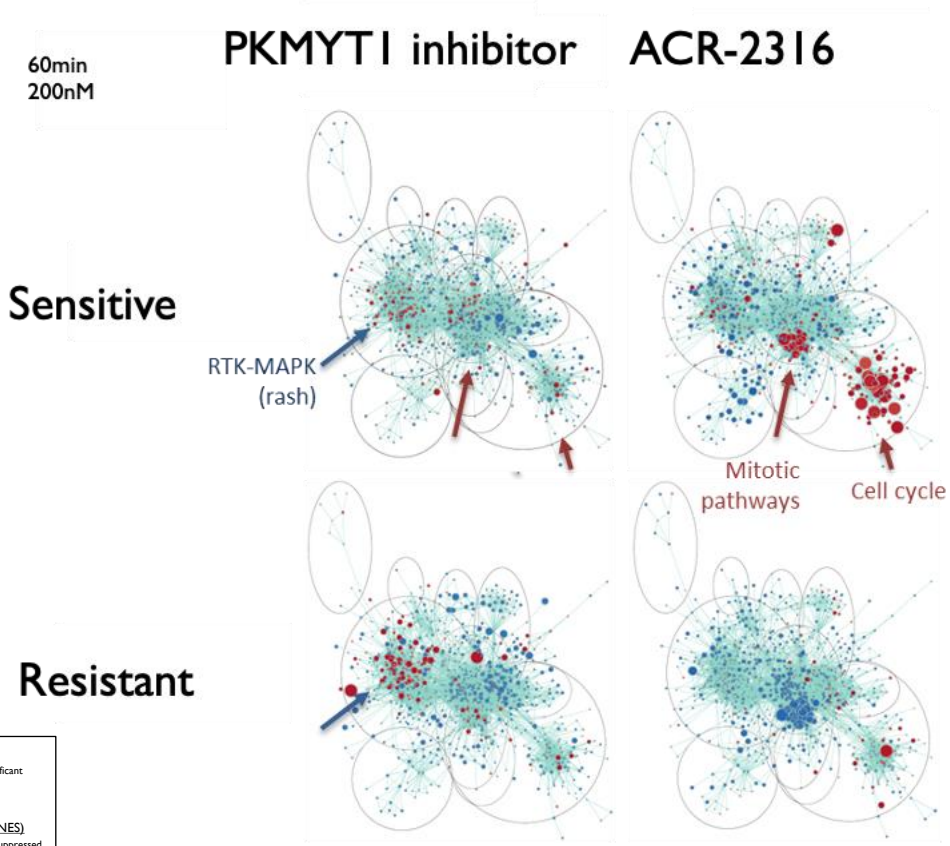
Resistant

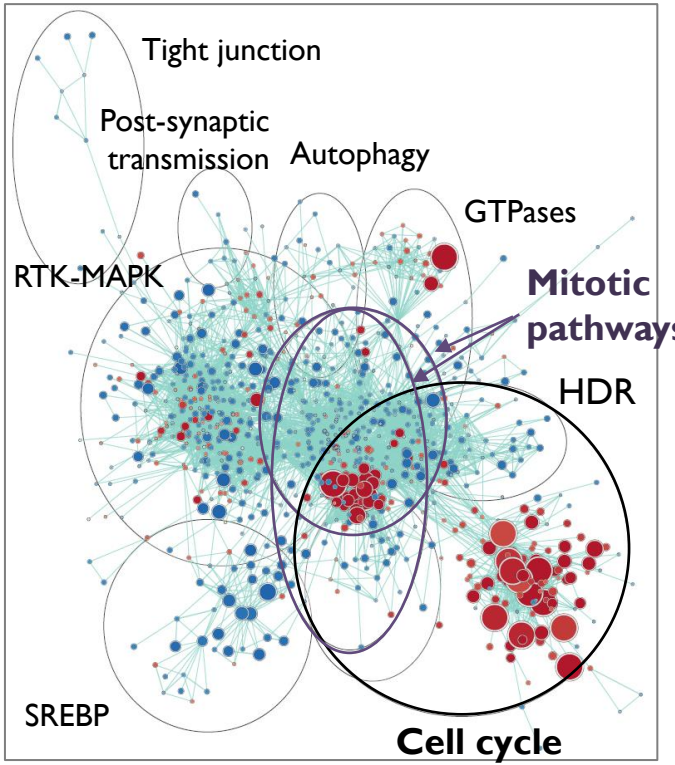






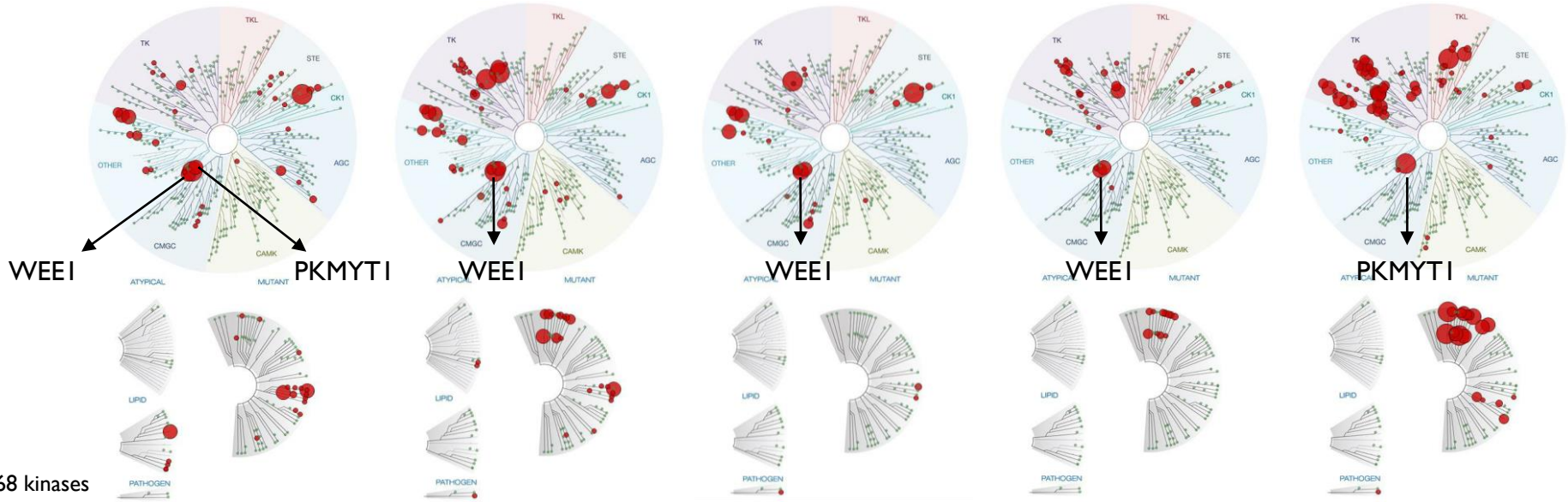
AP3 ANALYSIS: ACR-2316 REGULATES CELL CYCLE AND MITOSIS MORE POTENTLY THAN BENCHMARK PKMYT1 INHIBITOR





COMPREHENSIVE KINOME SELECTIVITY PROFILING

ACR-2316 | Adavosertib | Azenosertib | Debio0123 | Lunresertib



WEE1 PKMYT1 | WEE1 | WEE1 | WEE1 PKMYT1

468 kinases
@ 1μM

Percent Control
0%
0.1%
0.1-1%
1-5%
5-10%
10-35%
> 35%

KinomeScan

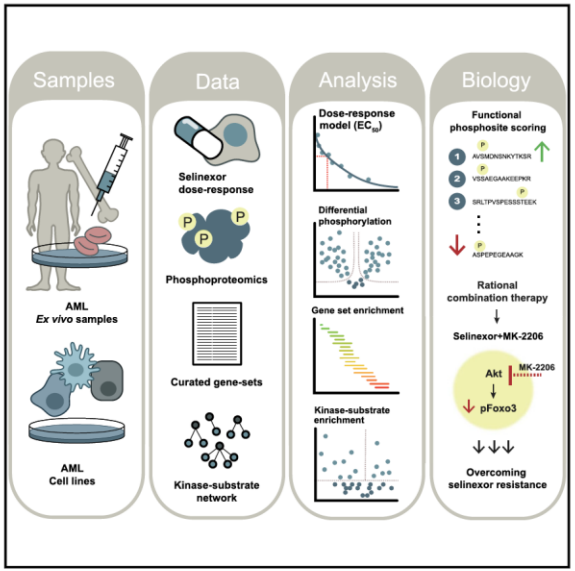
AP3 REVEALS SINGLE AGENT SENSITIVITY CONTEXT AND RATIONAL DRUG COMBINATIONS INDEPENDENT OF GENETIC INFORMATION

Article

Cell Reports

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

Graphical abstract



Authors

Kristina B. Emdal, Nicolàs Palacio-Escat, Caroline Wigerup, ..., Kristina Masson, Peter Blume-Jensen, Jesper V. Olsen

Correspondence

pub.saez@uni-heidelberg.de (J.S.-R.), kmasson@acrivon.com (K.M.), pblumejensen@acrivon.com (P.B.-J.), jesper.olsen@cpr.ku.dk (J.V.O.)

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