Acrivon Therapeutics

ACRIVON PREDICTIVE PRECISION PROTEOMICS (AP3)

OVERCOMING LIMITATIONS OF GENETICS-BASED PRECISION MEDICINE

CORPORATE PRESENTATION

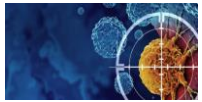
MARCH 2024

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.

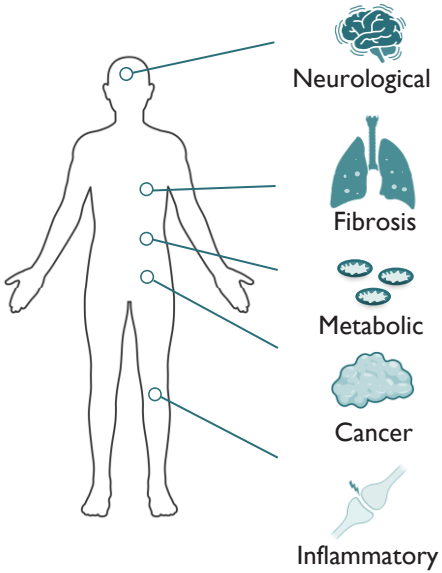
You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this presentation. We undertake no obligation to update any forward-looking statements or to reflect new information or the occurrence of unanticipated events, except as required by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

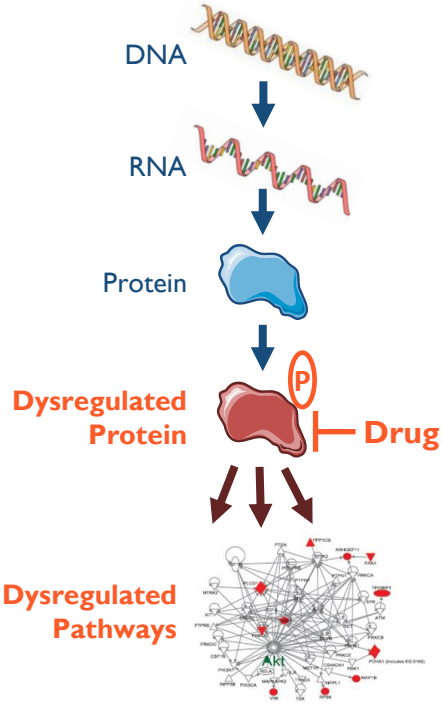
CRITICAL CHALLENGES FACING BIOPHARMA INDUSTRY

	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

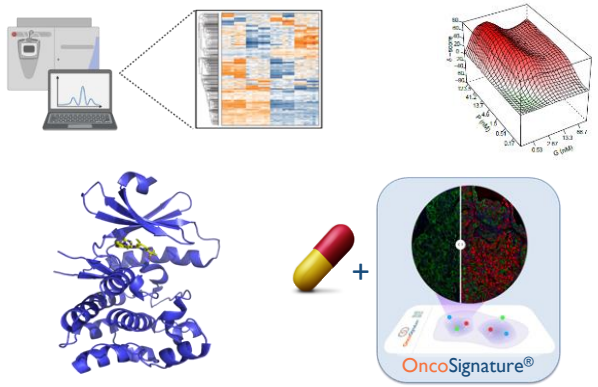
ACRIVON THERAPEUTICS – A NEXT-GENERATION PRECISION MEDICINE COMPANY





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 (SAR, resistance, patient responders); leveraged for internal pipeline



ACRIVON THERAPEUTICS AT A GLANCE

OVERCOMING LIMITATIONS OF GENETICS-BASED PRECISION MEDICINE

ACR-368 (Phase 2)
CHK1/2 inhibitor in registrational intent trials in multiple solid tumor types

ACR-2316 (IND-enabling)
Dual WEE1/PKMYT1 inhibitor with superior selectivity and single agent activity

Preclinical Drug Discovery
Additional AP3-enabled, co-crystallography-driven precision oncology programs

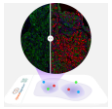
Drug Discovery
AP3-based SAR facilitated by co-crystallography

Clinically Actionable Resistance Mechanisms
Rational drug combinations

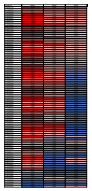
OncoSignature
Proprietary, drug-tailored patient responder identification tests

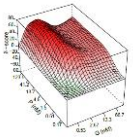
Experienced team focused on execution with cash runway into 2H 2025

AP3: MULTIPLE PROVEN DELIVERABLES ACROSS R&D



OncoSignature®





Clinical Biomarkers
Predictive OncoSignature tests

Indication Finding
Sensitive tumor types

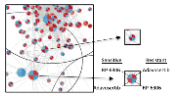
Resistance Mechanisms
Rational drug combinations

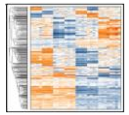
AP3

Drug Discovery SAR
Optimal target selectivity

PD Markers
~6,000 per compound

Informs in-licensing
AP3 profiling of candidates

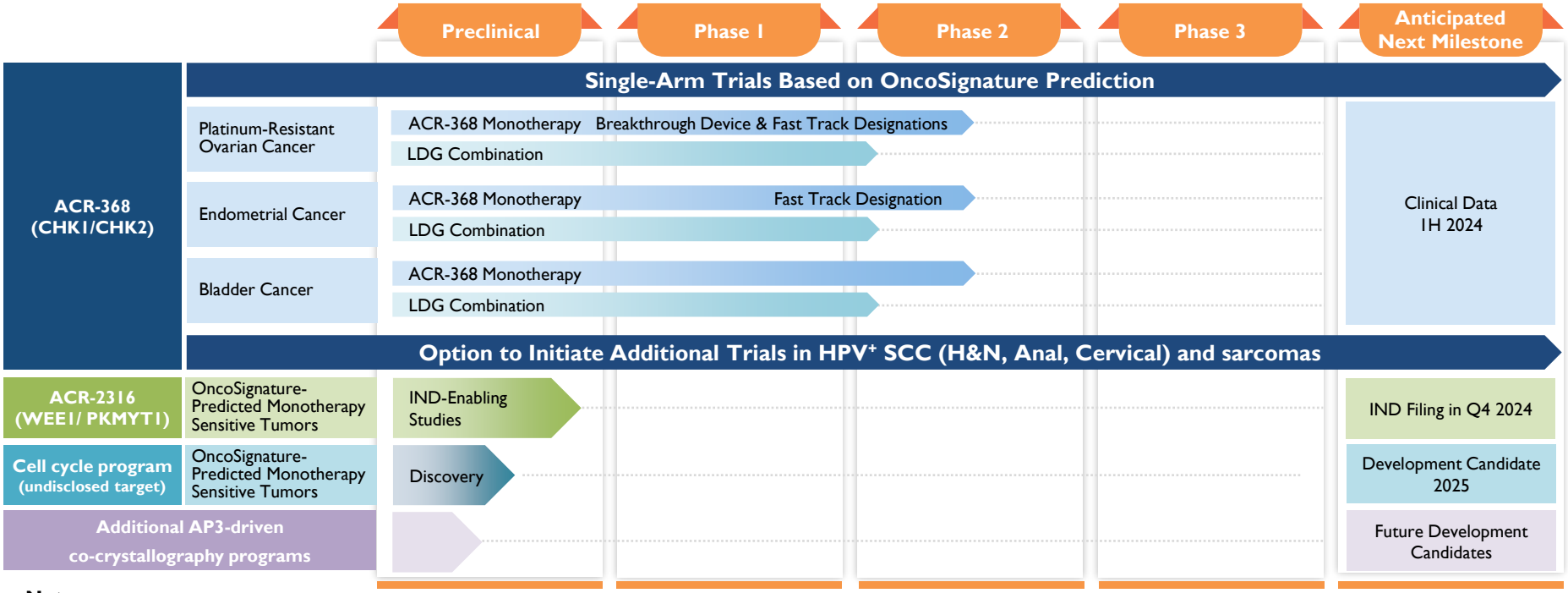




Intellectual Property
De novo exclusivity & protection against generics

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

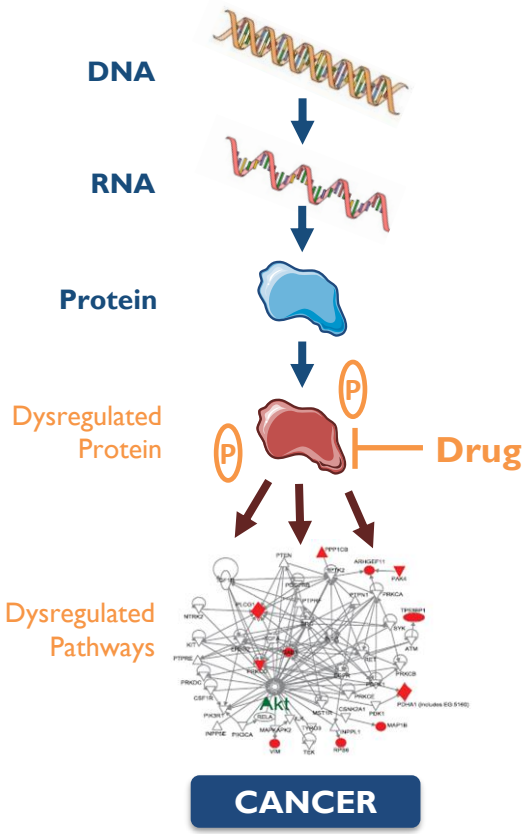
Erick Gamelin, M.D., Ph.D.
Chief Development Officer

- 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 APPLIED TO ONCOLOGY



Genomic Biomarkers are useful for patient selection in the smaller subset of cancers (<10%) with single gene driver mutations or known synthetic lethal context*

CANCER IS CAUSED BY DYSREGULATED PROTEIN ACTIVITY

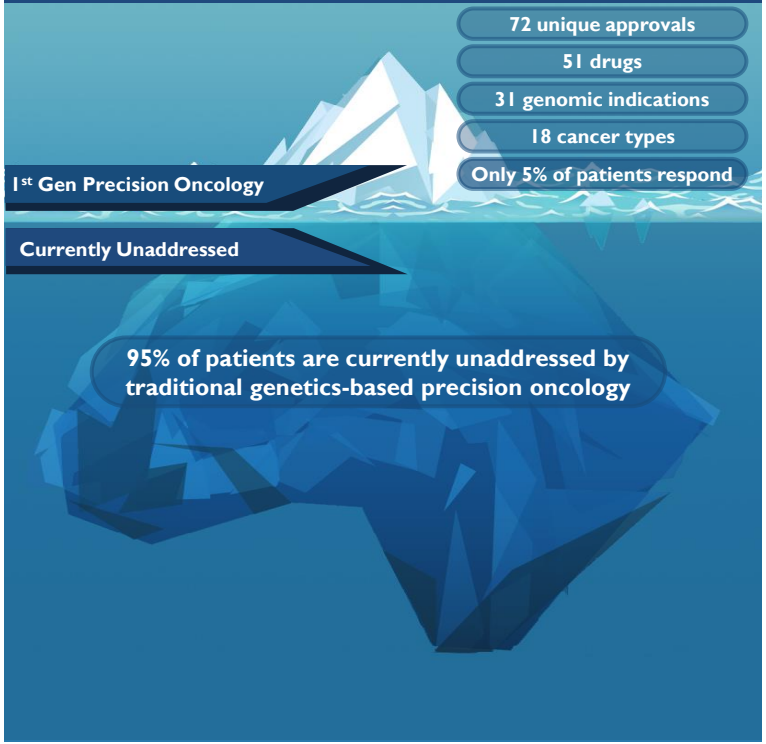
Acrivon's AP3 platform directly measure the disease-driving, dysregulated proteins and is designed to enable an exact match with the drug mechanism-of-action independent of genetic alterations

(Acrivon meaning: "*Exact, Accurate*")

**Oncogenic Kinase Signaling: Blume-Jensen, P. and Hunter, T. Nature (2001)*
Synthetic lethality as an engine for cancer drug target discovery: Huang, A. et al. NatRevDrugDisc (2020)

AP3 PLATFORM ADDRESSES HIGH UNMET NEED BEYOND NGS-BASED PRECISION MEDICINE

Current Precision Oncology Approaches Only Scratching the Surface



Acrivon Positioned to Increase Precision Oncology Market Size

Precision Oncology 1.0

Herceptin trastuzumab
Approved indications:
HER2+ Breast Cancer
HER2+ Gastric Cancer

gleevec imatinib mesylate
Approved indications:
CML (BCR-ABL)
Ph+ ALL

Precision Oncology 2.0

LOXO ONCOLOGY
Solid Tumors (NTRK))

agios
IDH mutation in AML

ignyta
NSCLC (NTRK) and CRC (ROS1, ALK)

MIRATI THERAPEUTICS
NSCLC (KRAS G12C)

TYRA
Bladder (FGFR3)

KINNATE BIOPHARMA
Class II and III BRAF kinase alterations: N/A

ELEVATION ONCOLOGY
Solid Tumors (NRG1)

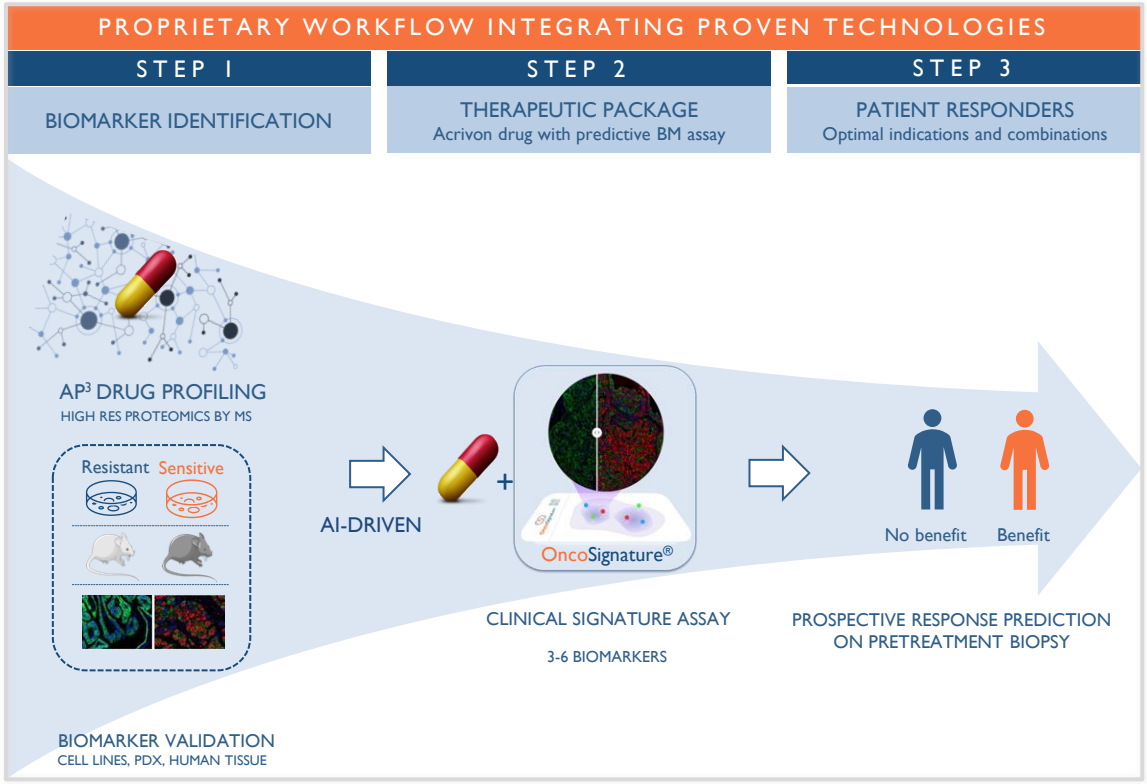
Predictive Precision Proteomics

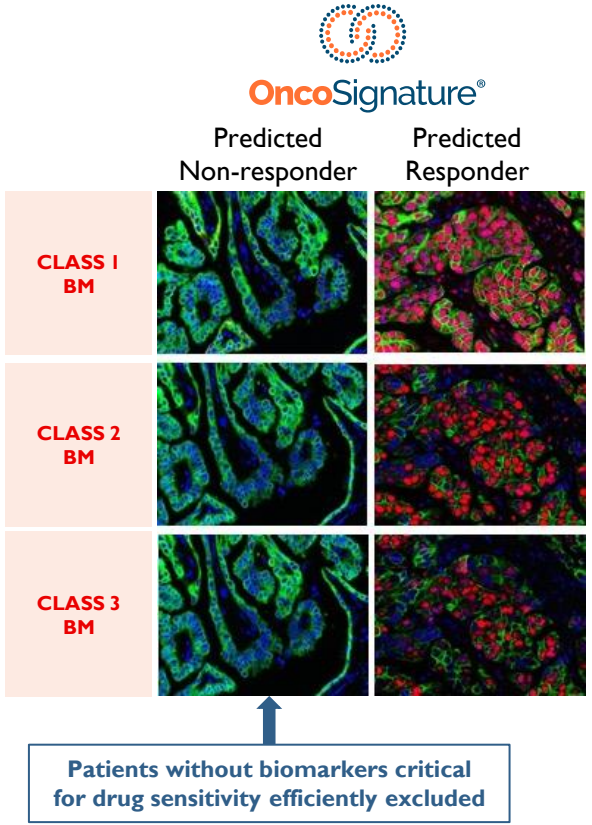
Acrivon Therapeutics

Aiming to make targeted therapeutic solutions available to broader group of cancer patients

Sources: Company Filings, ACS, CDC, NCI, Wall Street Research (2022)

AP3 PLATFORM: DRUG RESPONSE PREDICTION IN INDIVIDUAL PATIENTS

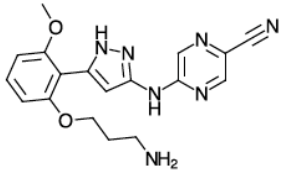




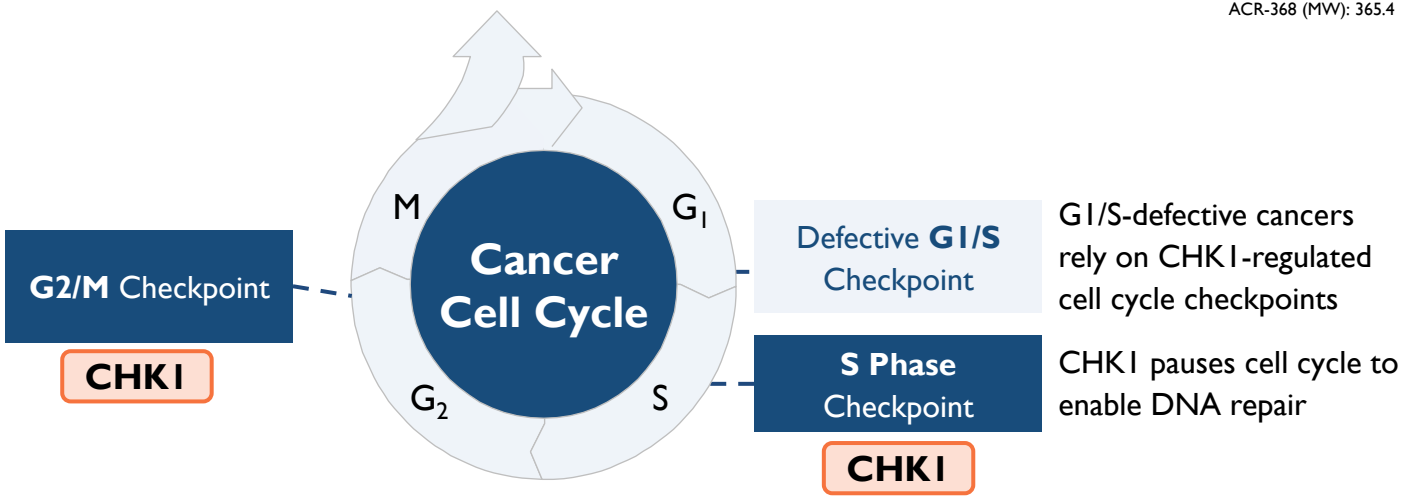
"Disease Pathway-Based Method to Generate Biomarker Panels Tailored to Specific Therapeutics for Individualized Treatments": EP 2 229 589, issued June 10, 2015; US2017/0067877A9, pending. OncoSignature® *is a Registered Trademark: US Reg. No. 5,718,472; Int. Cl. 5, 42. Intl. Reg. 1382289*

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



- **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 ACR-368 MONOTHERAPY (PAST DATA)

Indication	Trial	ORR# (confirmed)	Median DoR°	Reference
HGSOC* (BRCA wild type, primarily platinum-resistant)	Phase 2 single center (NCI)	29%	>10 months^	Lee et al, Lancet Oncology, 2018
HGSOC (BRCA wild type and mutant; platinum-resistant and refractory)	Phase 2 multi-center (Lilly)	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 (Lilly)	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%

*High grade serous ovarian cancer; ^Updated post-publication; # Overall response rate; °Duration of Response

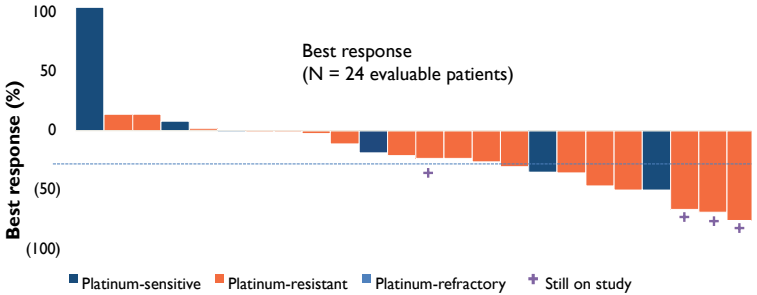
PAST PHASE 2 TRIALS IN HIGH GRADE SEROUS OVARIAN CANCER

NCI single-center Phase 2 study (N=28)

- Heavily pre-treated patients; median 5 prior lines
- Pretreatment tumor biopsies mandated

RESULTS

- ORR 29%; mDoR >10 months (post-publication)
- No genetic correlation with p53^{mut}, DDR^{mut}, or CCNE1



Lee et al; Lancet Oncology: 2018

Lilly-sponsored multi-center (46 center, 8 country) Phase 2 study (N=169)

- All lines of prior therapy, BRCA wt and mt, incl. prior PARPi
- Pretreatment tumor biopsies mandated

RESULTS

- ORR 12.1% (excl. unconfirmed); mDoR =5.6 months
- No correlation with genetic alterations

N = 169 PATIENTS	COHORT DESCRIPTION	PERCENT CONFIRMED ORR (95 % C.I.)
Cohort 1 (53)	Plat resistant BRCA wt; ≥3 lines of prior therapy	11.3 (4.3 to 23.0)
Cohort 2 (46)	Plat resistant BRCA wt; < 3 lines of prior therapy	13.0 (4.9 to 26.3)
Cohort 3 (41)	Plat resistant BRCA mt, any line of therapy (must include prior PARPi)	12.2 (4.1 to 26.2)
Cohort 4 (29)	Plat refractory, any BRCA, any line of therapy	6.9 (0.8 to 22.8)

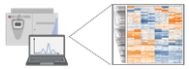
Konstantinopoulos et al; Gynec. Oncol.: 2022

- ✓ Past trials suggest unenriched all-comer ORR in HGS ovarian cancer is ~15-20%
- ✓ Durable clinical activity in most responders
- ✓ No predictive biomarkers identified, need for alternative biomarker approach (ideal for AP3)

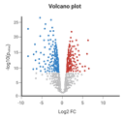
DEVELOPMENT OF AP3-BASED PATIENT SELECTION ONCOSIGNATURE TESTS

P-proteomics

Quantitative mapping >60,000 p-sites; 25% drug-related



Drug-regulated phospho-sites and biological processes

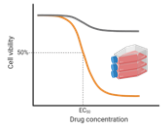


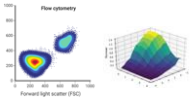
Pathway visualization and reconstitution

Literature and database mining

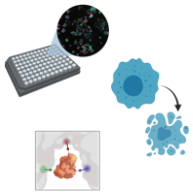
Cellular MOA

Dose response, knockdowns, drug combinations



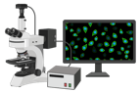


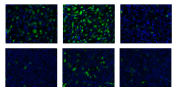
Target engagement, cell assays, imaging

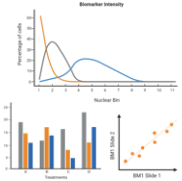


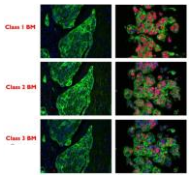
Technical Validation (Intended use tissue)

BM antibody validation by quantitative IF on human and PDX samples

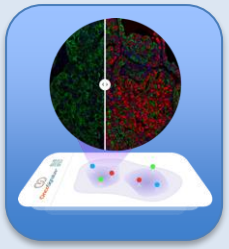








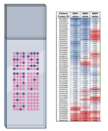
Final OncoSignature Assay



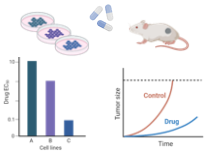
OncoSignature®

Functional Validation (Intended use tissue)

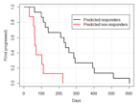
Human cancer screening: ID of drug-sensitive cancers and proportions of responders



Prediction of drug sensitivity in cancer cell lines and PDX models

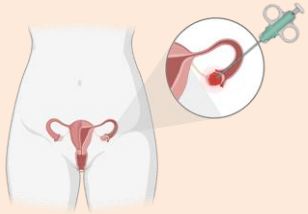


Patient responder prediction on pre-treatment tumor biopsies

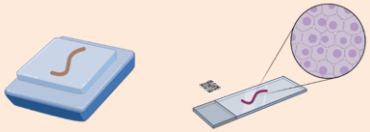


ACR-368 ONCOSIGNATURE TEST: USAGE IN THE CLINIC

Pretreatment tumor biopsy

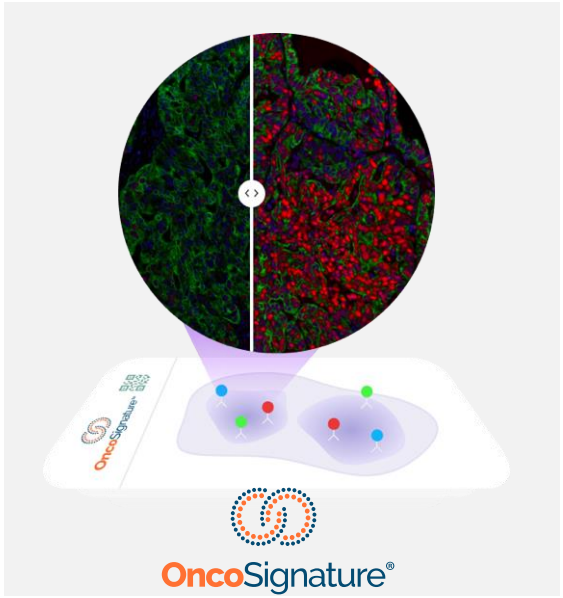


Sample processing



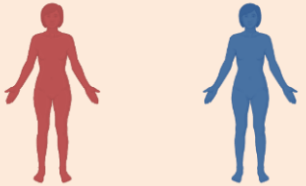
Biopsy in FFPE block

Automated tumor Region-of-Interest biomarker scoring



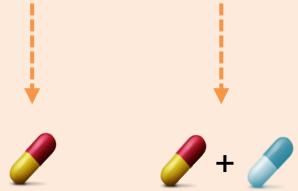
- Pretreatment tumor biopsy test
- Compatible with 5 business days turn-around
- Offered by CDx partner under exclusive license from Acrivon

Treatment decision based on patient stratification



OncoSignature-positive

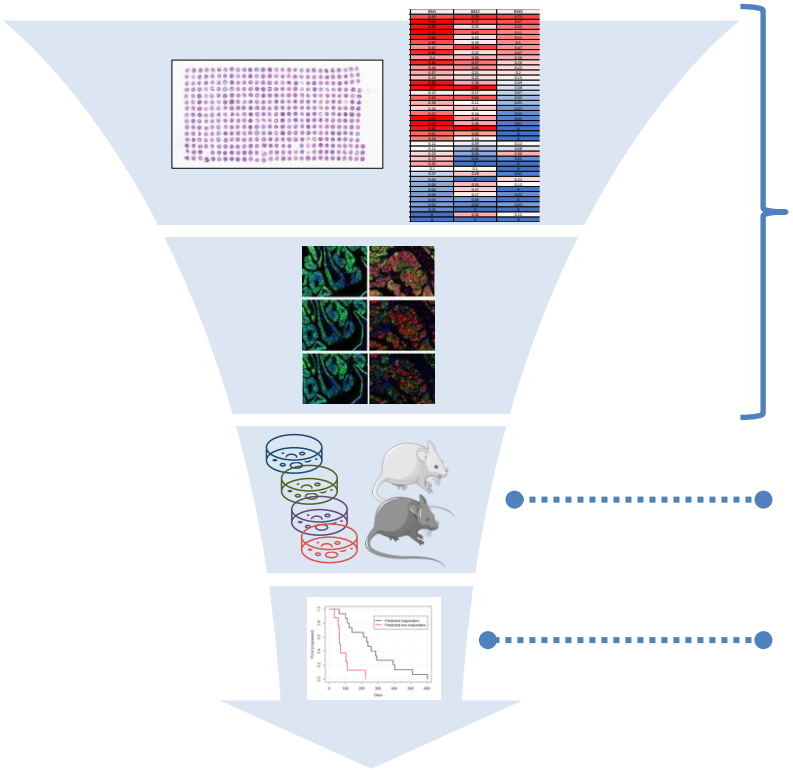
OncoSignature-negative



ACR-368 monotherapy

ACR-368 + LDG combination

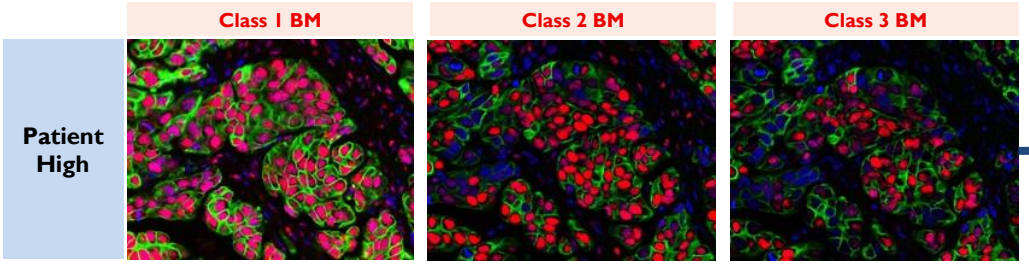
CONSISTENT ACR-368 ONCOSIGNATURE PERFORMANCE ACROSS PRECLINICAL STUDIES



OncoSignature®

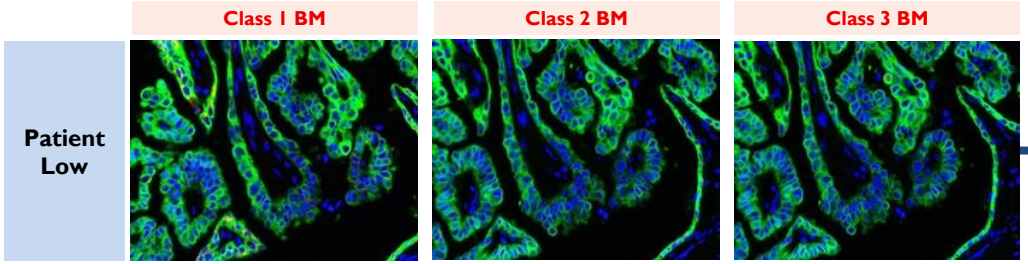
- Prediction of the fraction of human tumors sensitive to single agent ACR-368
  - Selection rate 30-40% across lead indications
- Identification of additional human tumor types predicted sensitive to single agent ACR-368
  - Endometrial and bladder cancer
- Prediction of treatment outcome in human PDX 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®

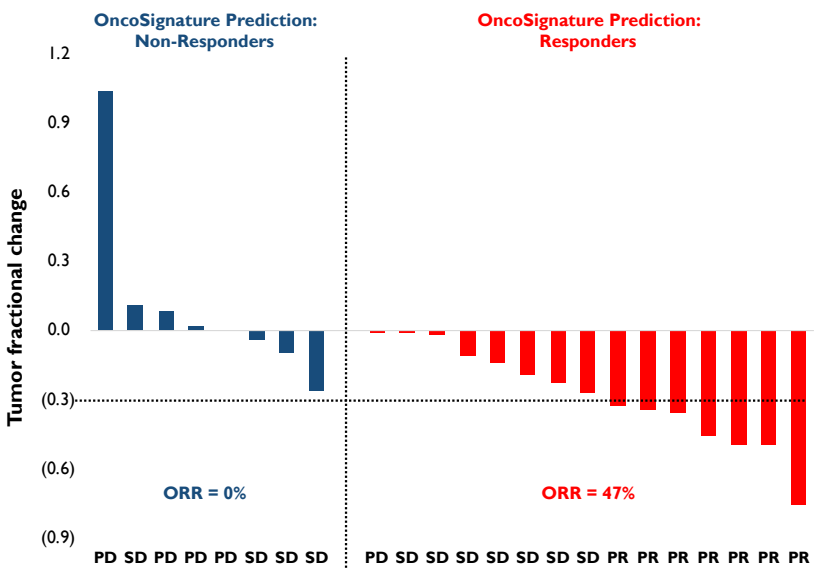


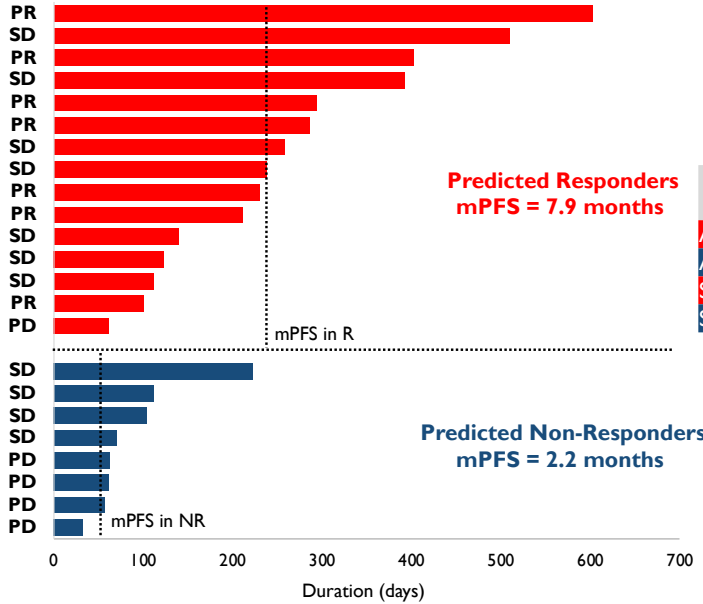
Predicted Non-Responder
Patient with no drug target dependency efficiently excluded

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	0.76	0.64	0.75
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	0.38	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	0.77	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	0.87	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	0.90	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	0.96	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	0.00
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

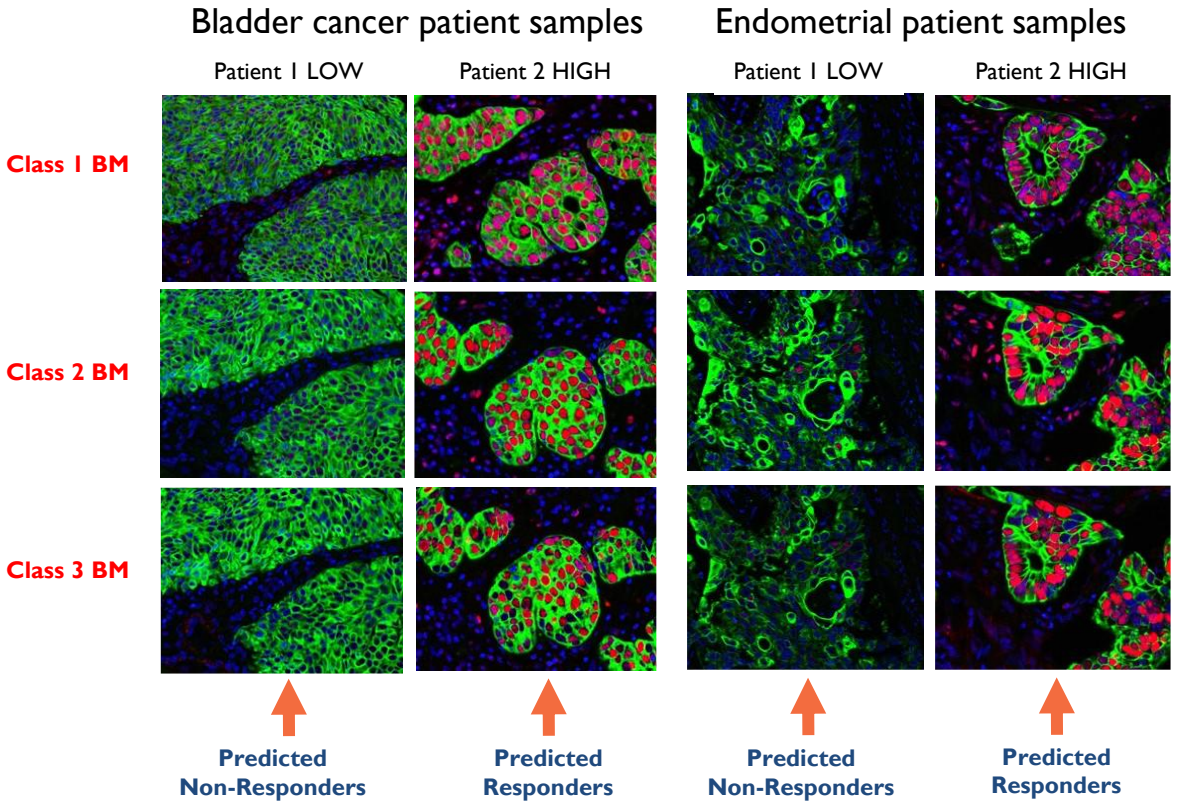
OncoSignature-positive = 30-50%

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%

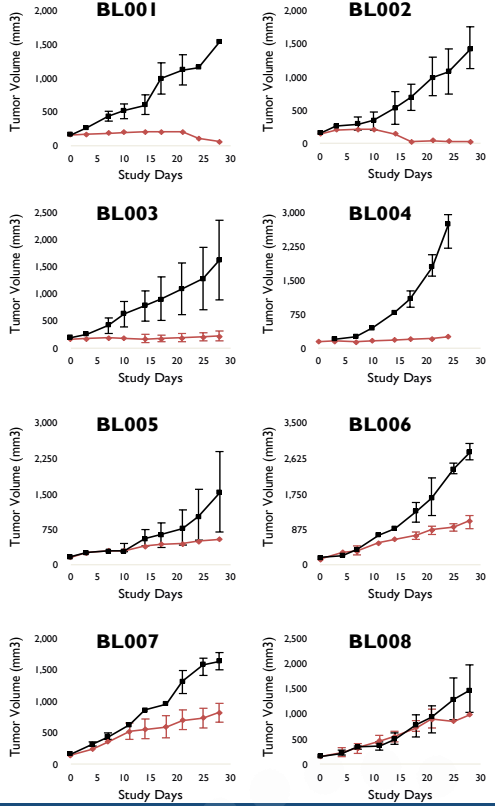
TWO ATTRACTIVE ACR-368-SENSITIVE CANCER TYPES IDENTIFIED



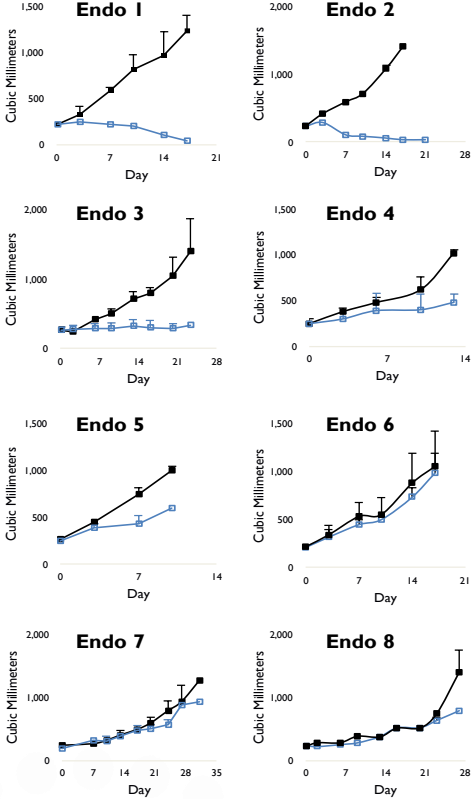
ACR-368 OncoSignature screening of human cancer samples

A SUBSET OF ENDOMETRIAL AND BLADDER PDX MODELS ARE HIGHLY SENSITIVE TO ACR-368

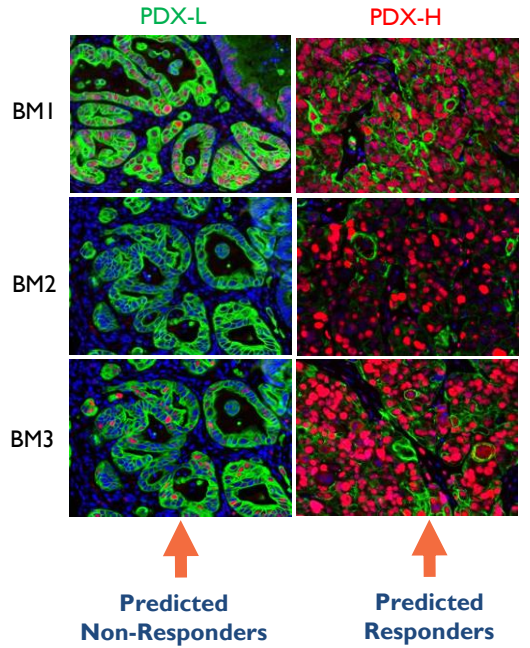
Bladder PDX



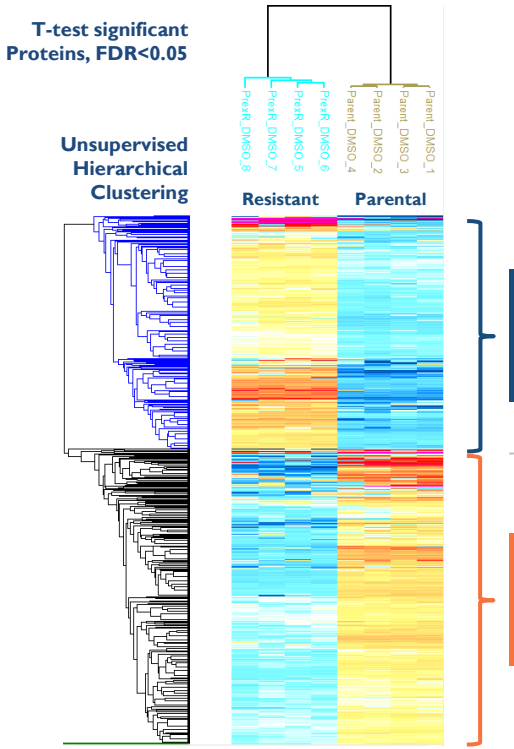
Endometrial PDX



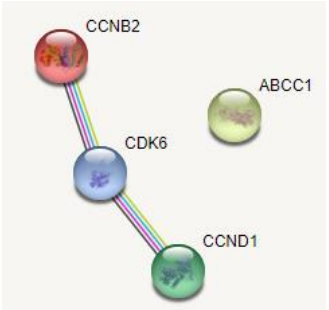
ACR-368-sensitive responders



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

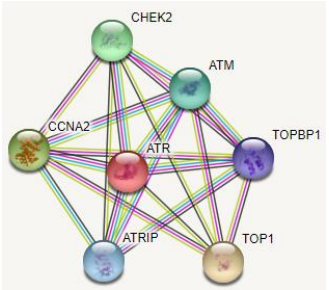


Upregulated in ACR-368 Resistant Cells



G1/S CELL CYCLE

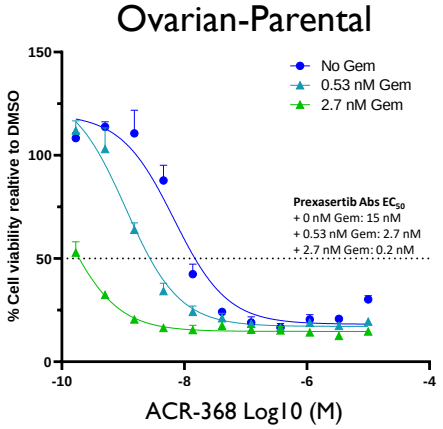
Downregulated in ACR-368 Resistant Cells

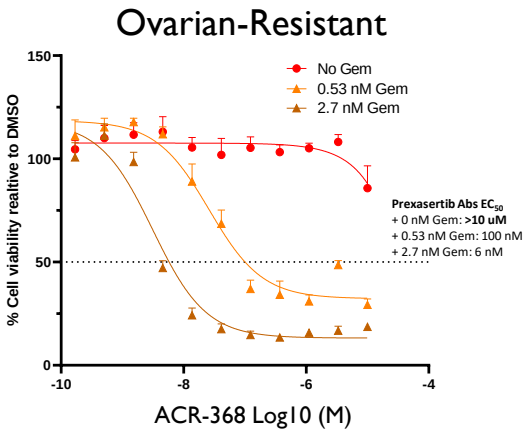


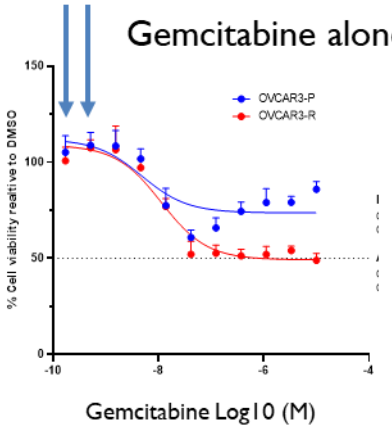
DNA DAMAGE REPAIR

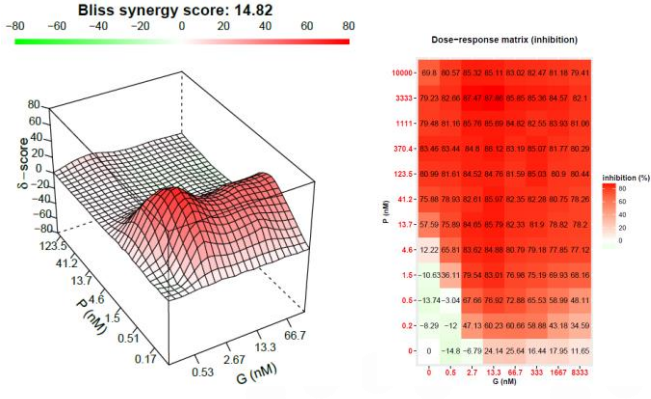
Data suggest that gemcitabine might be a rational combination to overcome DDR suppression

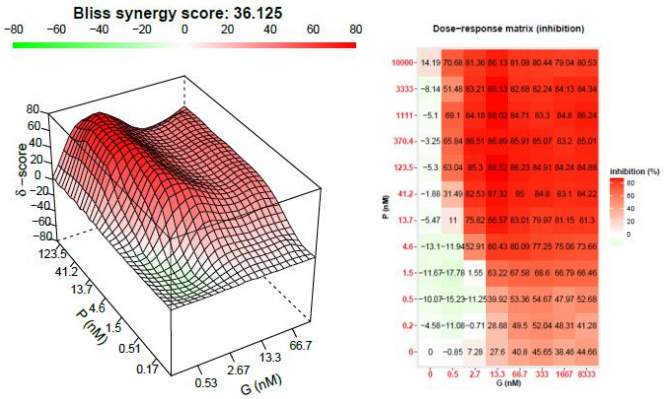
LOW DOSE GEMCITABINE SENSITIZES OVARIAN CANCER CELL LINES TO ACR-368









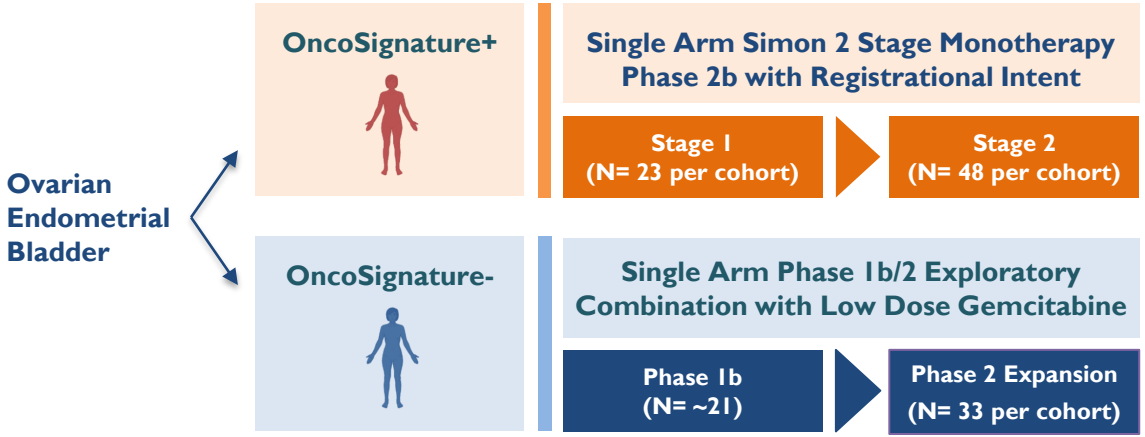


Bliss Synergy score:

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

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
- 66 sites currently 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

INITIAL CLINICAL OBSERVATIONS SUPPORT AP3 PREDICTIONS AND PAST TRIAL SAFETY DATA

- Consistent with the extensive experience and tolerability profile from past trials, drug-related adverse events are primarily hematological, reversible, and manageable

- In the limited number of patients evaluated by imaging, preliminary evidence of clinical activity has been observed in OncoSignature-positive patients across all three tumor types treated with single agent ACR-368 at RP2D

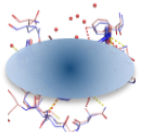
- Consistent with AP3-predicted tumor sensitivity, early imaging-based evidence of clinical activity across all three tumor types was also observed in OncoSignature-negative patients treated with ACR-368 at RP2D and LDG during the dose escalation phase

As disclosed in 10-Q filing November 9, 2023

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

ACR-2316 and DDR programs

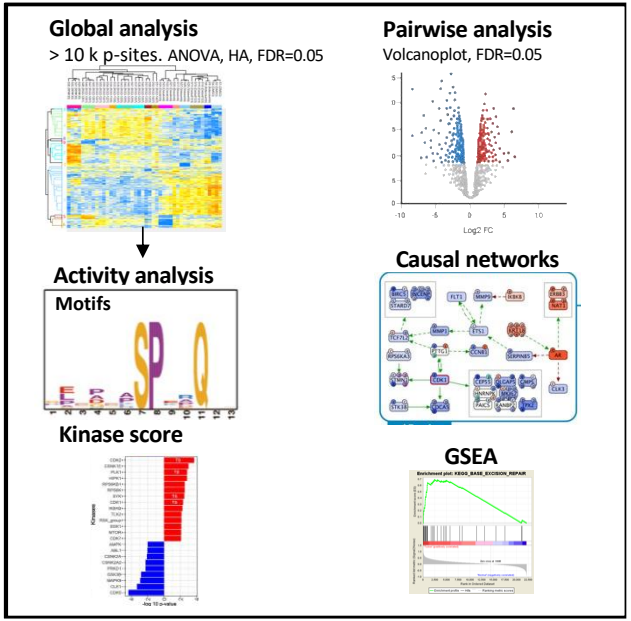
- >40 high resolution co-crystals (1.5-3.1 Å) and novel WEE1- and PKMYT1-selective structural series and lead candidates
- ACR-2316 a novel, potent, selective dual inhibitor
- Designed by AP3 to overcome WEE1 and PKMYT1 single inhibitor resistance
- IND target date Q4 2024



Cell cycle inhibitor program with undisclosed target

- Anticipated development candidate 2025

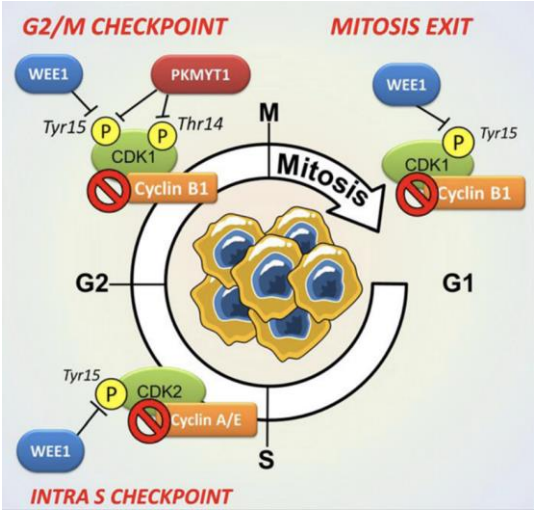
High throughput AP3 profiling



AP3 used for biologically relevant selectivity profiling

WEE1 AND PKMYT1 VALIDATED 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
- WEE1 inhibition propagates genomic instability by premature DNA replication and cell cycle progression, resulting in mitotic catastrophe
- PKMYT1 inhibition results in premature mitotic entry and cell death
- Strong preclinical data and emerging clinical data



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

- ✓ Single agent clinical activity (WEE1 and PKMYT1)
- ✓ Correlation with genetic alterations challenging, CCNE1 association being explored by others
- ✓ Acrivon intends to leverage OncoSignature for optimal patient selection

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

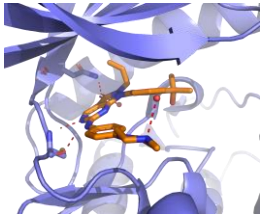
Program goals:

- **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

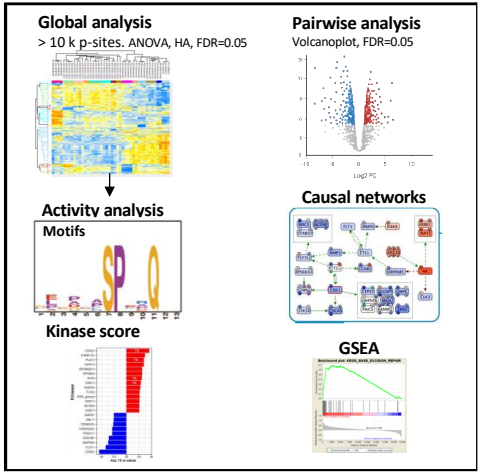
- ✓ 5-20-fold more potent in preclinical models than clinical benchmarks
- ✓ Superior anti-tumor efficacy with complete tumor regression across models
- ✓ High selectivity ensures transient, short-lived, mild AEs
- ✓ Potent WEE1 inhibition, balanced PKMYT1 inhibition, overcomes resistance

Co-crystallography for drug design and selectivity

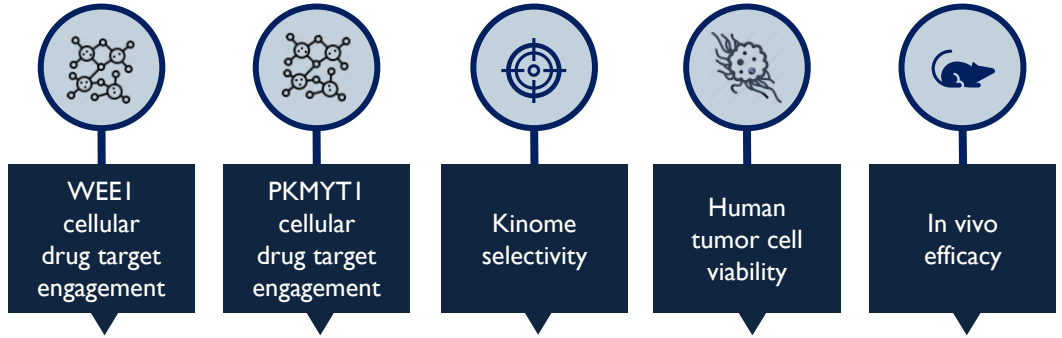


Zhu et al, J. Med. Chem. (2017)

AP3 used for biologically optimal SAR



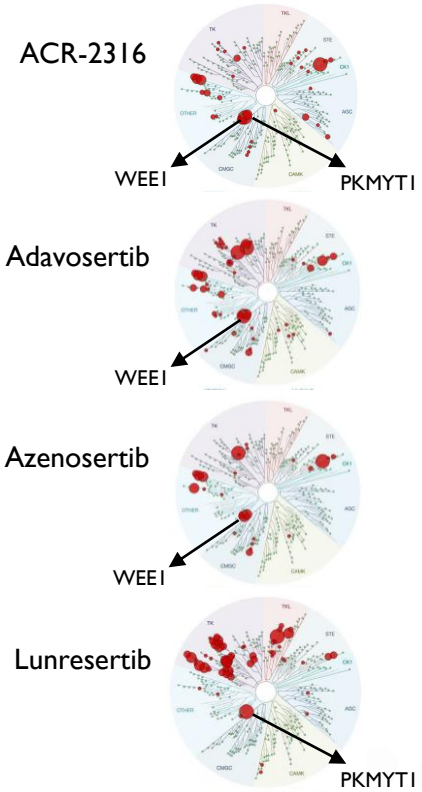
ACR-2316 SHOWS ATTRACTIVE PROFILE IN ONGOING PRECLINICAL STUDIES



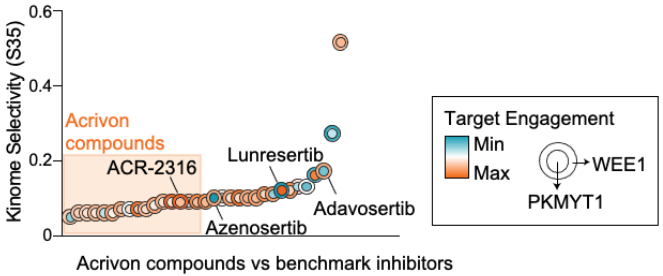
Relative performance	WEE1 cellular drug target engagement	PKMYT1 cellular drug target engagement	Kinome selectivity	Human tumor cell viability	In vivo efficacy
ACR-2316	**++++**	**++**	**++++**	**++++**	**++++**
Adavosertib	++	-	++	+++	++
Azenosertib	++	-	+++	++	++
Debio0123	+	-	++++	+	+
Lunresertib	-	+++	+	+	+

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

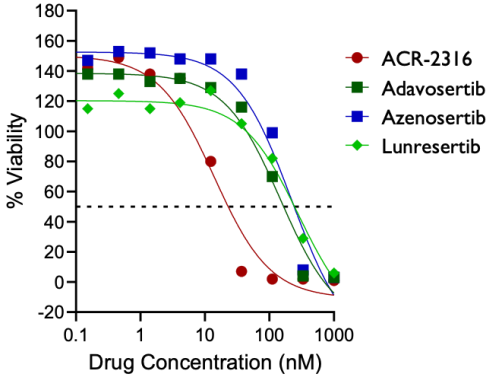
KinomeScan (468 kinases @ 1μM)



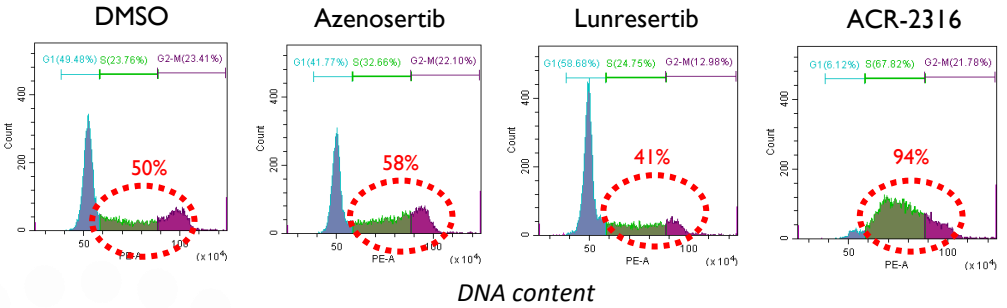
ACR-2316 is highly selective (KinomeScan)



ACR-2316 potently inhibits cancer cell viability



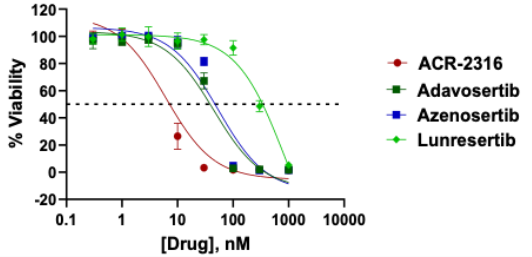
ACR-2316 exerts potent cell cycle effects with pronounced S-G2/M accumulation



100 nM, 24 hour

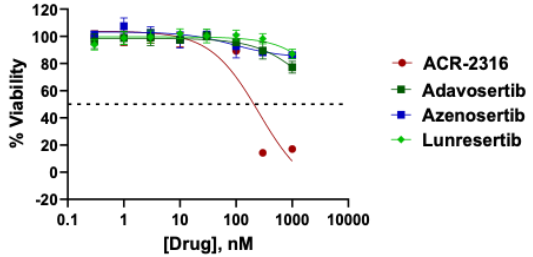
ACR-2316 SHOWS SUPERIOR ACTIVITY VS BENCHMARKS ACROSS ALL HUMAN TUMOR CELL LINES TESTED

Human Tumor Cell Line 1



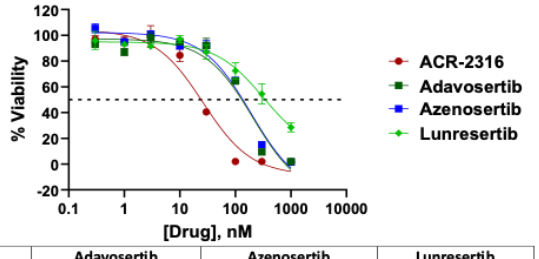
ACR-2316 IC50 (nM)	Adavosertib IC50 (nM)	Azenosertib IC50 (nM)	Lunresertib IC50 (nM)
7	39	47	340

Human Tumor Cell Line 2



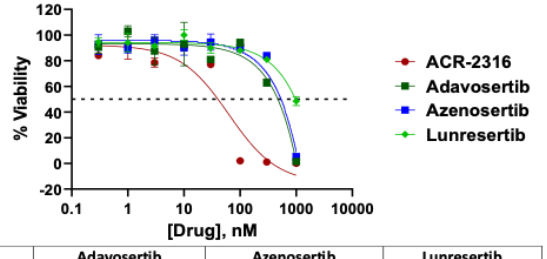
ACR-2316 IC50 (nM)	Adavosertib IC50 (nM)	Azenosertib IC50 (nM)	Lunresertib IC50 (nM)
207	> 1000	> 1000	> 1000

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



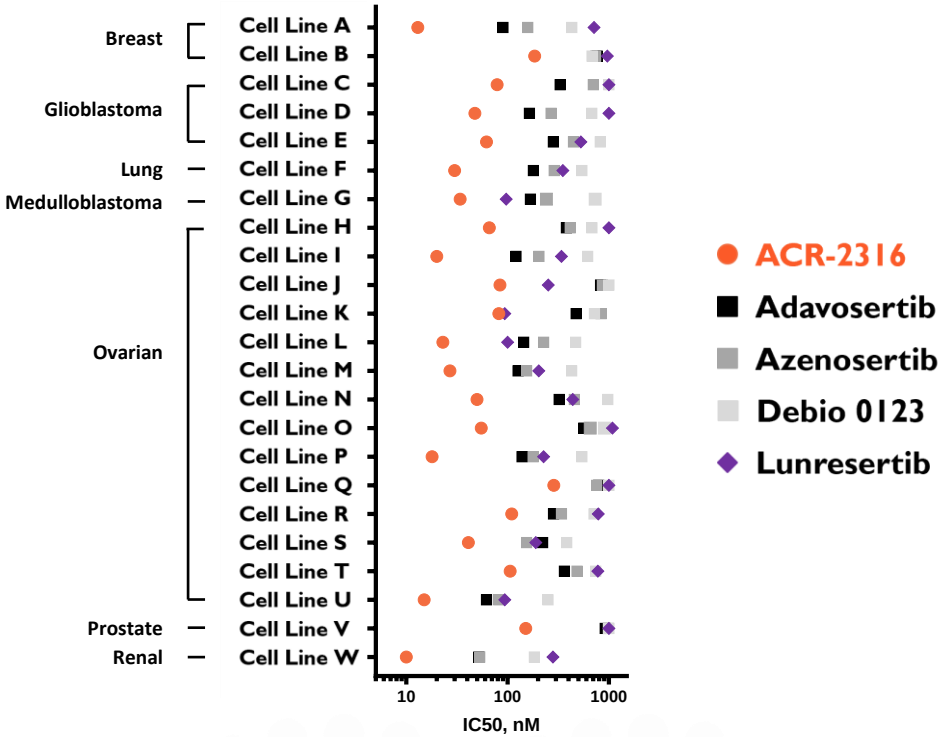
ACR-2316 IC50 (nM)	Adavosertib IC50 (nM)	Azenosertib IC50 (nM)	Lunresertib IC50 (nM)
40	471	533	967

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

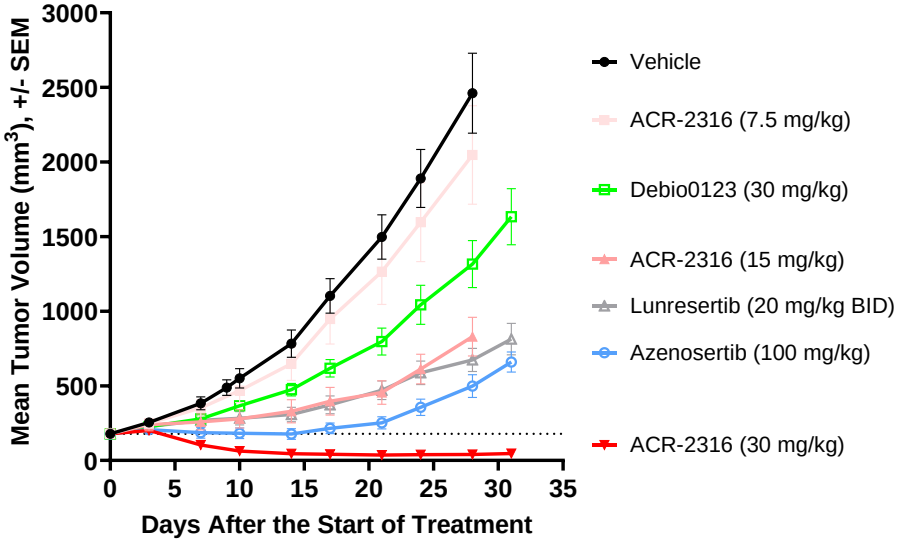
Human tumor cell lines



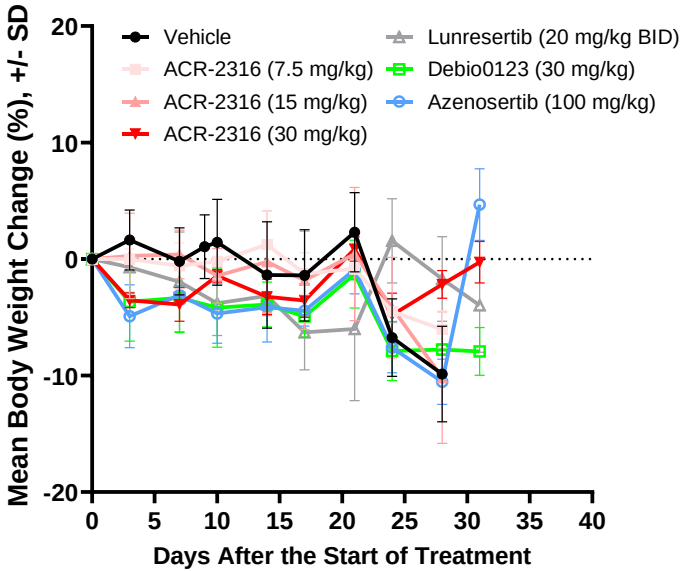
Patient-derived *ex vivo* tumor models

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

Efficacy (5d on/2d off)

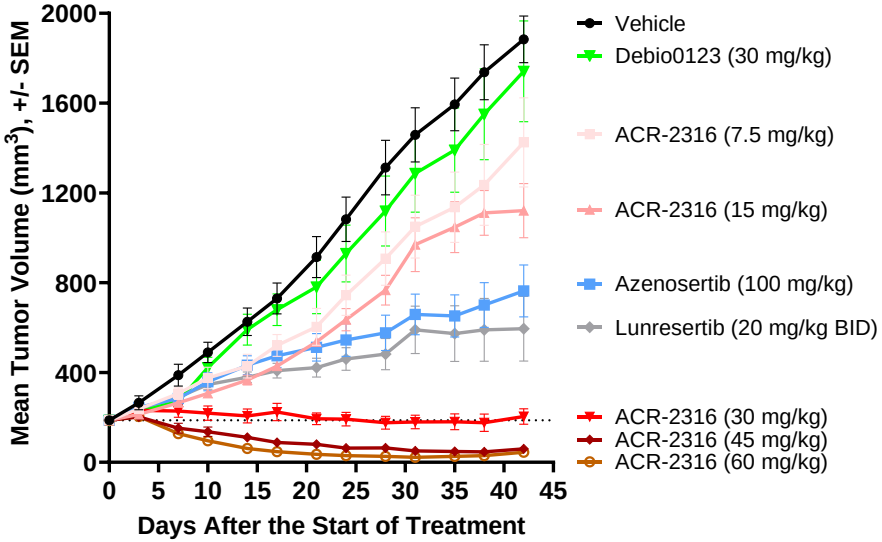


Tolerability (5d on/2d off)

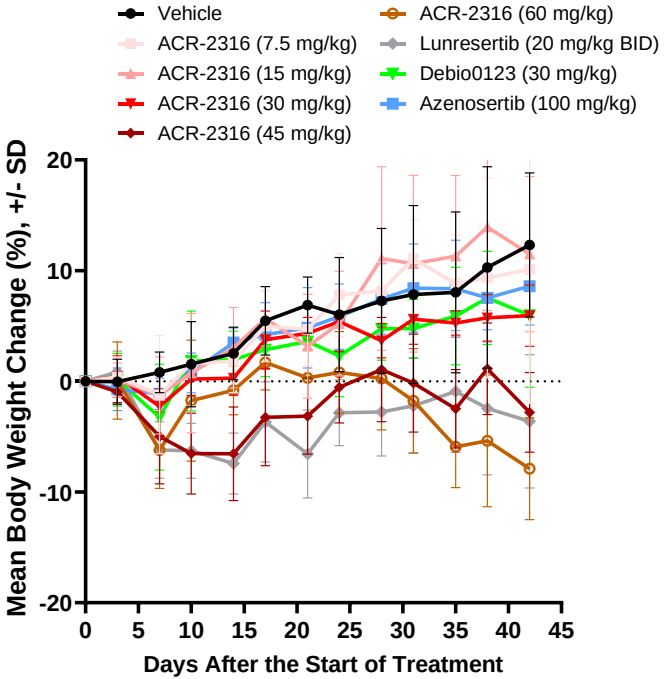


ACR-2316 SHOWS POTENT ANTI-TUMOR ACTIVITY COMPARED TO CLINICAL WEE1 OR PKMYT1 INHIBITORS – MODEL 2

Efficacy (5d on/2d off)

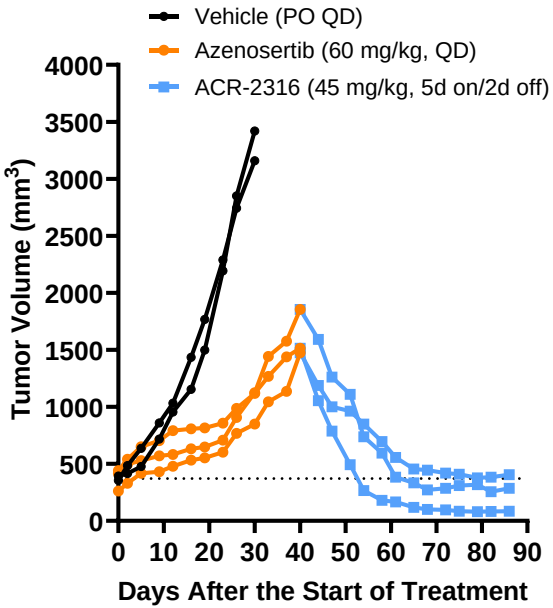


Tolerability (5d on/2d off)

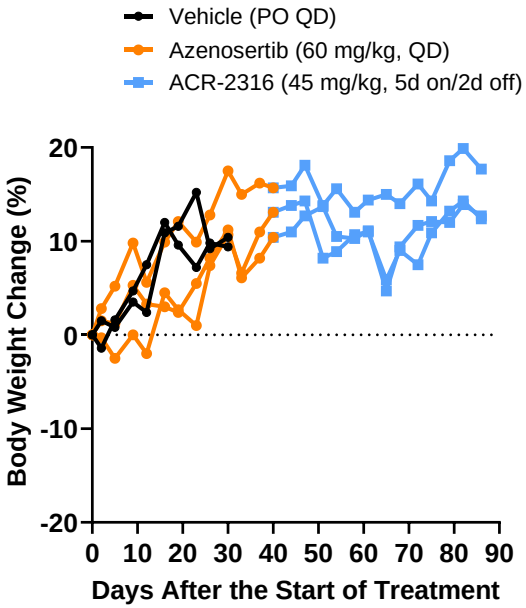


ACR-2316 SHOWS DEEP REGRESSION IN TUMORS PROGRESSING ON A BENCHMARK WEE1 INHIBITOR

Anti-tumor activity

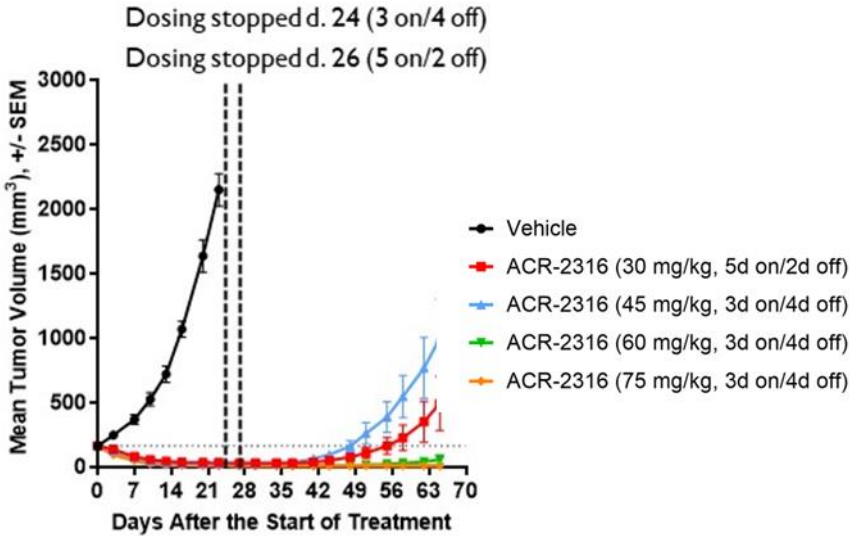


Tolerability

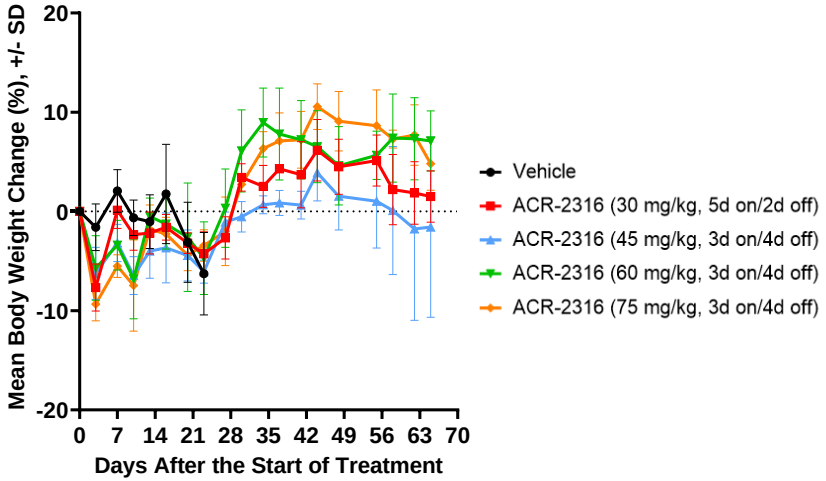


ACR-2316 LEADS TO POTENT AND DURABLE A427 TUMOR REGRESSION

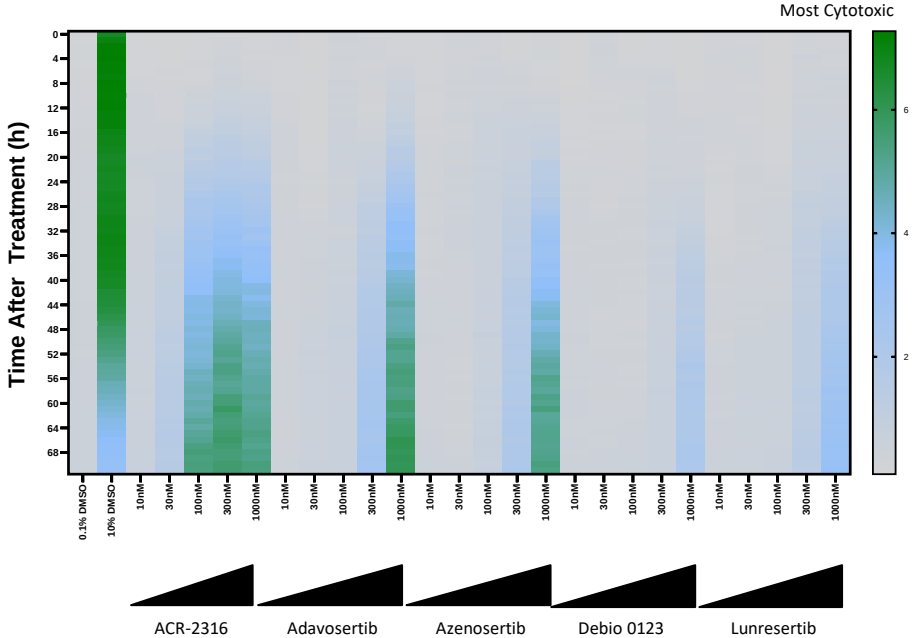
Efficacy

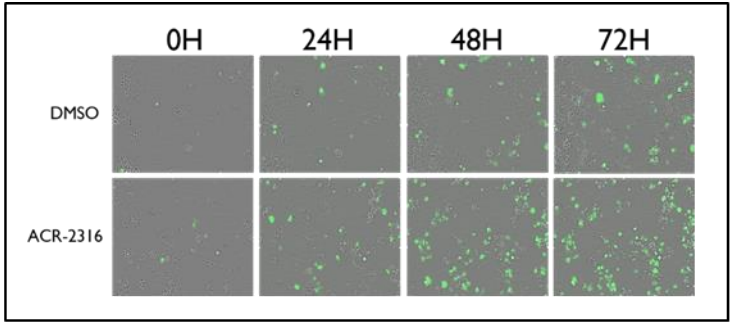


Tolerability



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

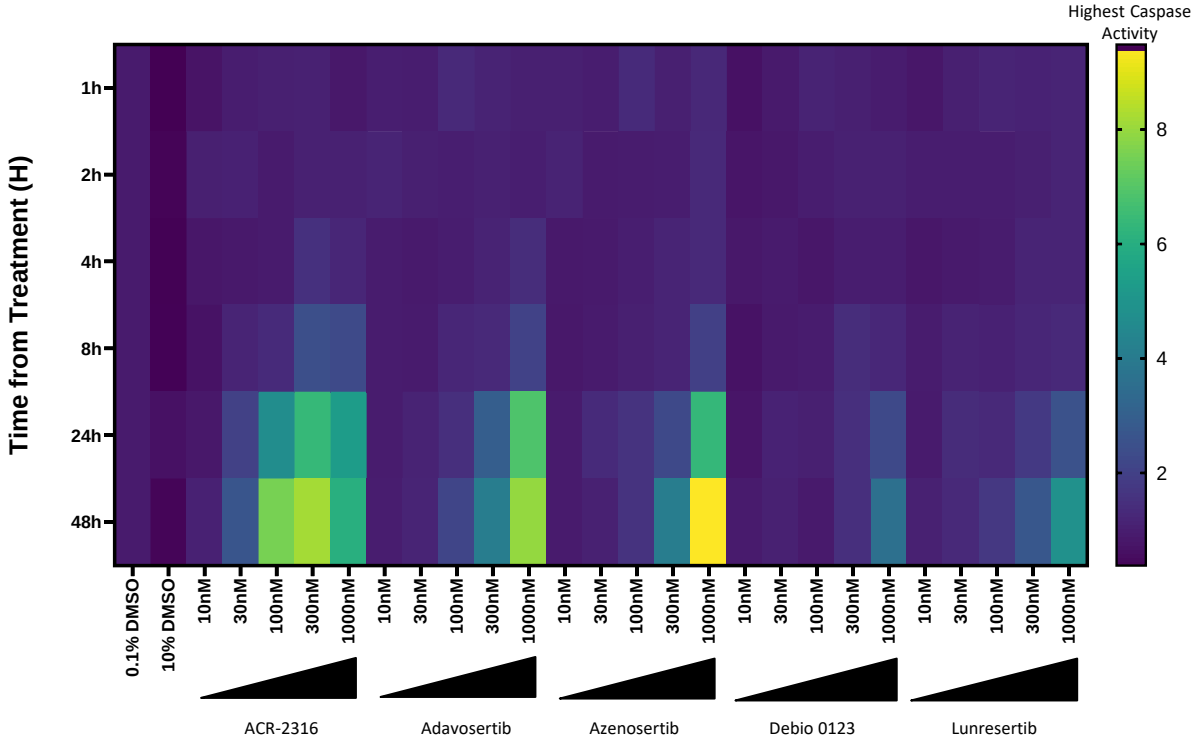




Representative images of OVCAR3 cells treated with 0.1% DMSO or 100 nM ACR-2316 (green fluorescence = dead cells)

CellTox-Green Assay (OVCAR3 Cells)

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:

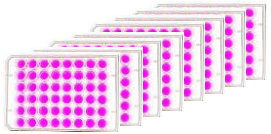
- ACR-2316 is well-tolerated, resulting in tumor regression in xenograft mouse models at multiple dosing regimens (qw, 2qw, 3d on/4d off, 5d on/2d off, and qd)
- Transient, reversible, mechanism-based hematological adverse events

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

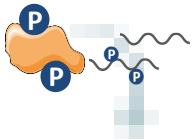
- MTD ≥ 30 mg/kg in both species (single dose)
- GLP tox studies (31 days) completed in rat and dog with the planned human dosing regimen achieving exposure required for tumor regression
- Minimal hematological effects in rats, except for mechanism-based transient, fully reversible reticulocytopenia 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

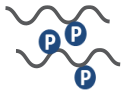
Drug treatment



Proteolysis
P-peptide enrichment

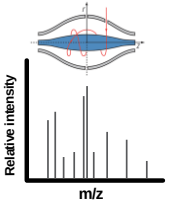


Peptide clean up



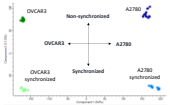
Ultra high resolution
P-proteomic profiling

Direct DIA analysis

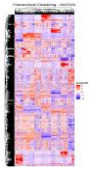


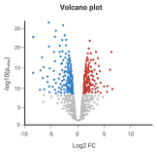
High resolution and throughput MS-based P-proteomics

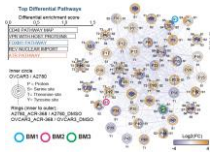
Quantitative mapping (>35,000 phospho-sites covering >4,500 proteins)



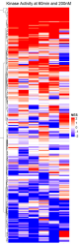
Drug-regulated phospho-sites and biological process enrichment

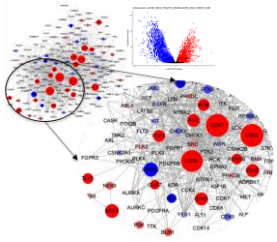


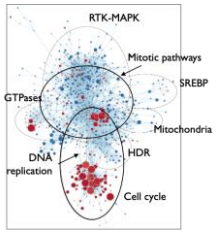




Drug-regulated pathway activity mapping and reconstitution







Proprietary pipe for automated AP3 analyses with actionable results

Week 0

Turnaround <2 weeks

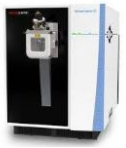
Week 2

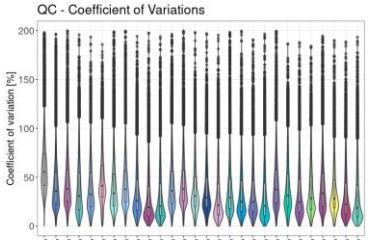
AP3: TIGHT, HIGH-RESOLUTION DATA WITH DEEP COVERAGE

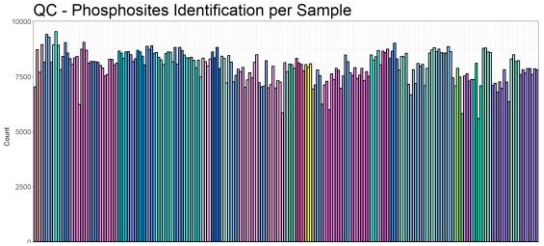
35388 p-sites

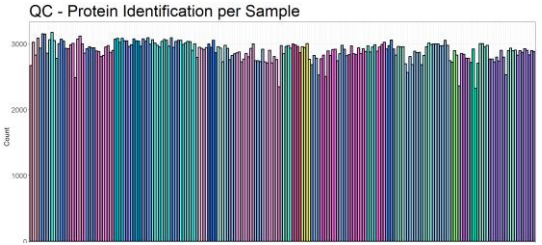
15733 p-sites

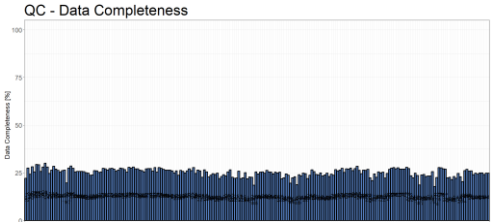
QC MS Data → Data Clean Up → QC Processed Data → Volcano Plots → Hierarchical Clustering → Consensus Sequence Motif → Kinase Inference → Pathway Enrichment → Functional Annotation → Network Mapping → Biomarkers

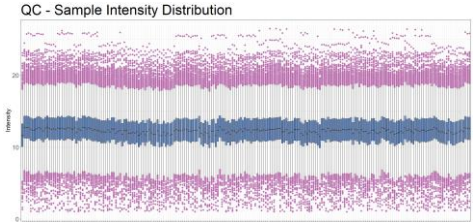


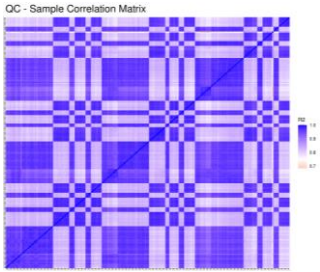






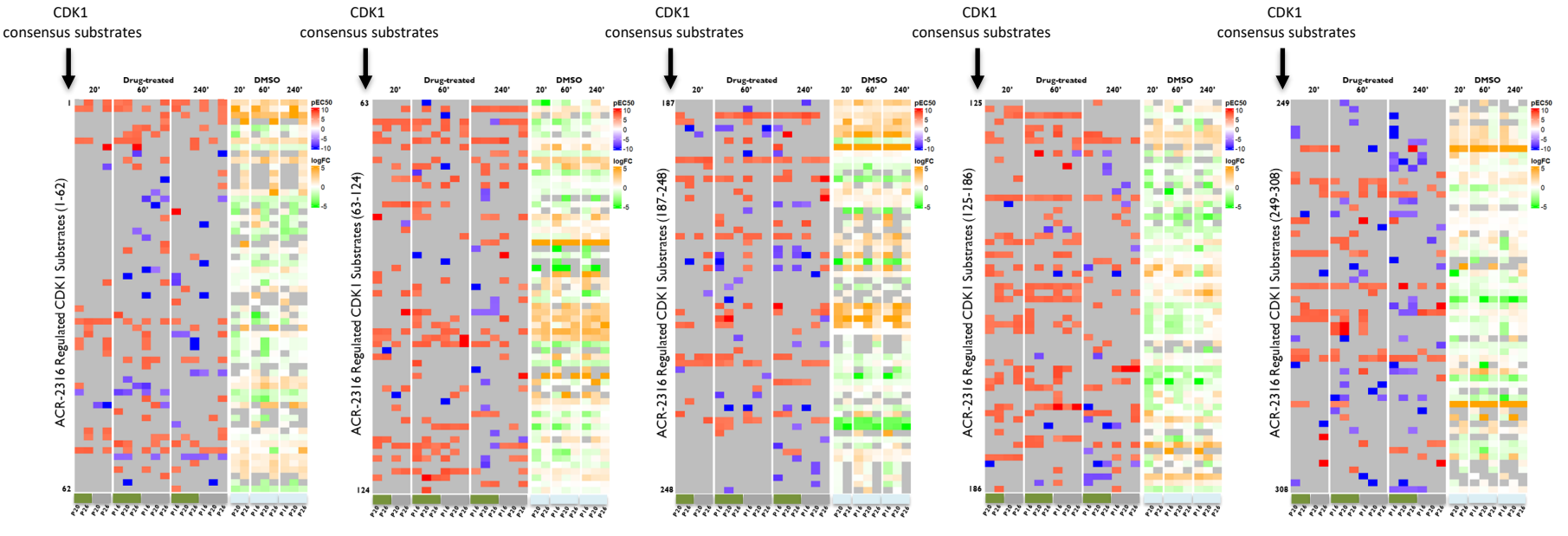






- ✓ Acrivon proprietary compound data (~50 million data points per experiment); dozens of compounds profiled
- ✓ Miniaturized, high throughput, scalable: <2 weeks turn-around, automated AI computational analyses in 1 day
- ✓ Actionable results: Resistance mechanisms, rational combinations, drug-tailored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

TIME- AND DOSE-DEPENDENT ACR-2316 MODULATED CDK1 SUBSTRATES (PD MARKERS) IN SENSITIVE AND RESISTANT TUMOR CELLS

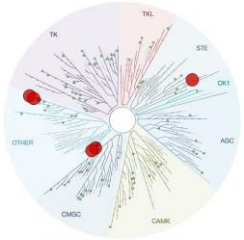


- Unbiased quantitation of ACR-2316-regulated CDK1 substrate p-sites (308) in intact cells based on CDK1 consensus recognition motif (Acrivon proprietary hybrid database approach) across multiple experiments

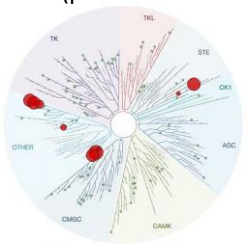
AP3 REVEALS DRUG-REGULATED KINASE ACTIVITY IN INTACT CELLS NOT DETECTABLE BY STANDARD METHODS

KinomeScan @ 1μM

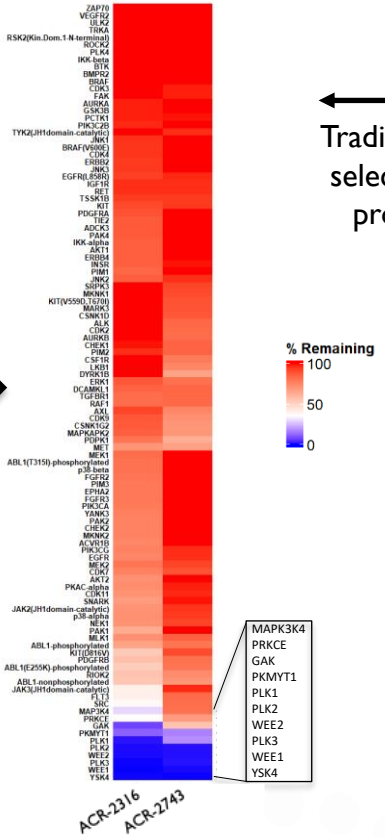
ACR-2316



ACR-2743 (previous lead candidate)



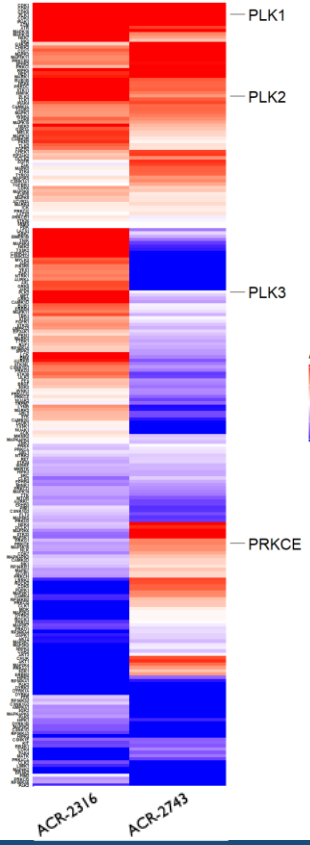
Time : 60 minutes
Dose : 20 nM

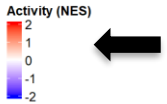


Traditional selectivity profiling

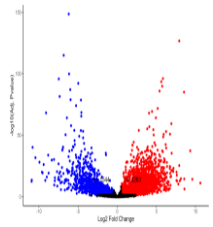
AP3-based pathway profiling

Drug-regulated kinase activity* in intact cells

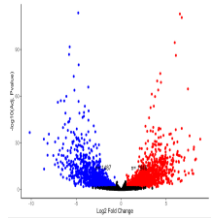




ACR-2316



ACR-2743

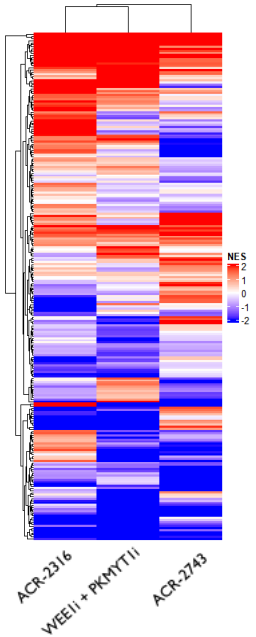


*Kinase activity based on substrate motif analysis using a proprietary PTM-SEA hybrid method

OPTIMIZED DUAL INHIBITORS SHOW DESIRABLE PATHWAY EFFECTS

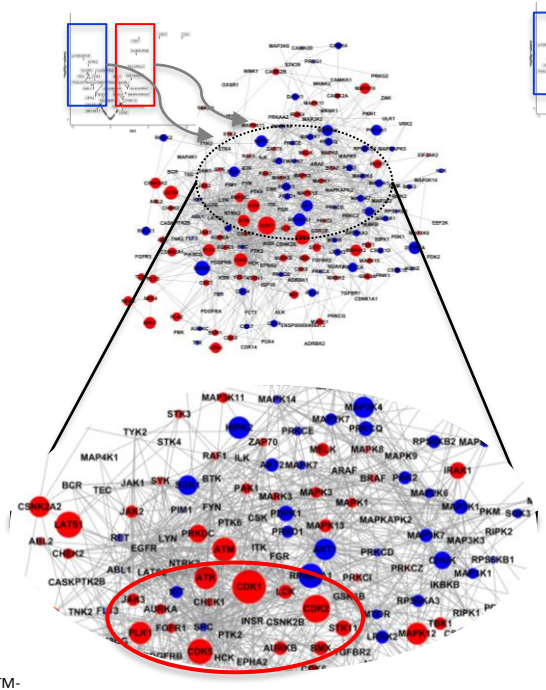
Optimized dual WEE1 and PKMYT1 inhibitors affect cell cycle and canonical MAPK pathways in desirable manner

Substrate motif-inferred kinase activities

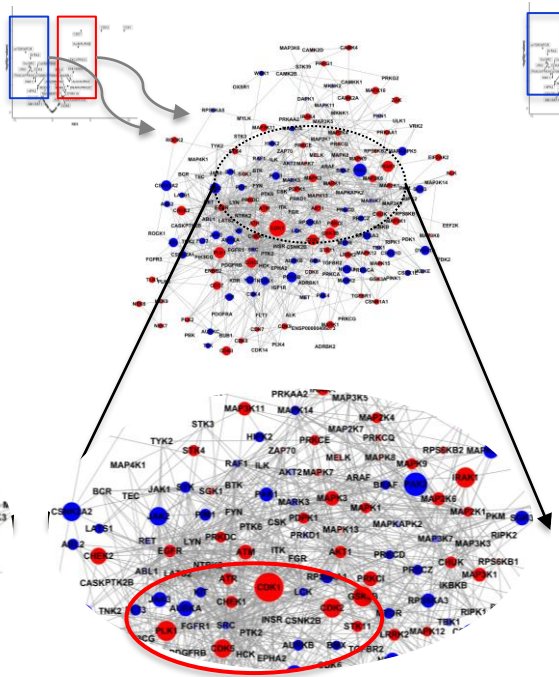


Kinase activity based on proprietary PTM-SEA-based hybrid workflow and analyses

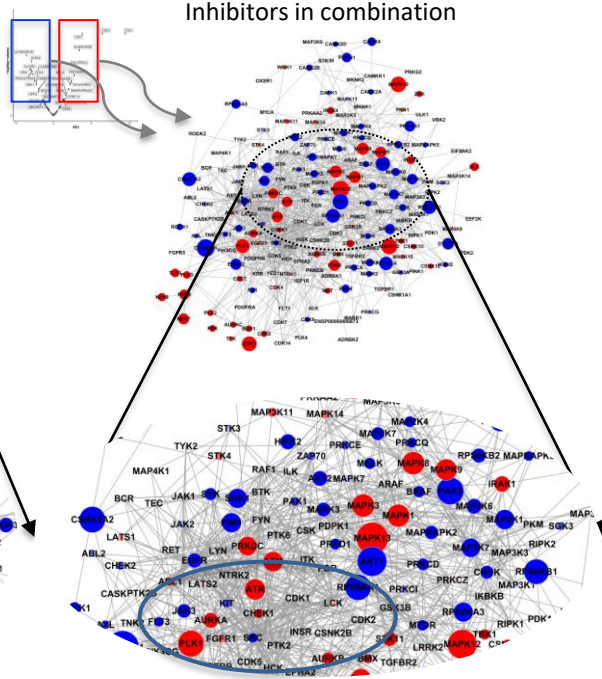
ACR-2316

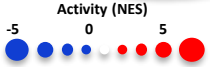


ACR-2743



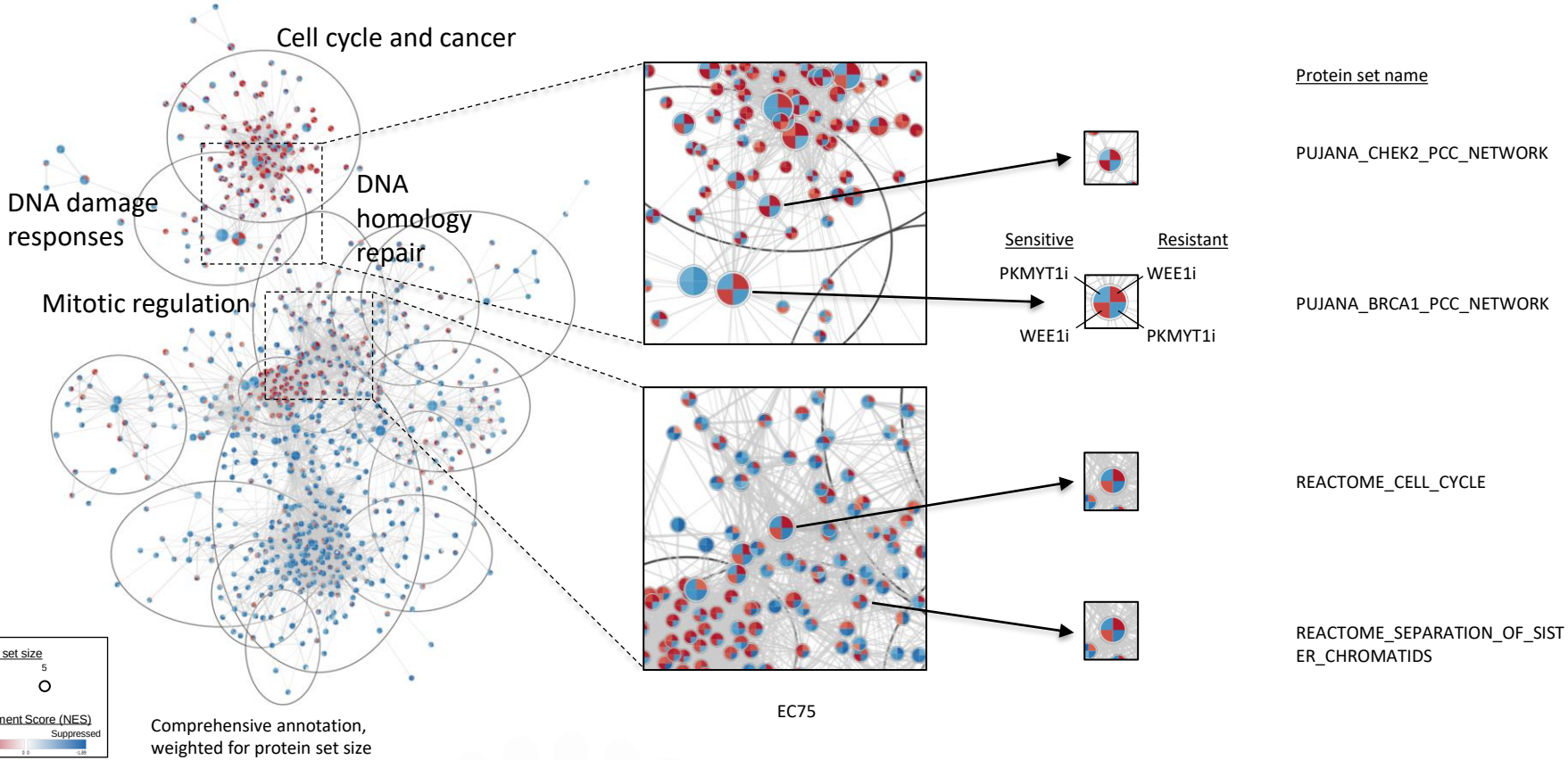
Benchmark* WEE1 + PKMYT1 Inhibitors in combination



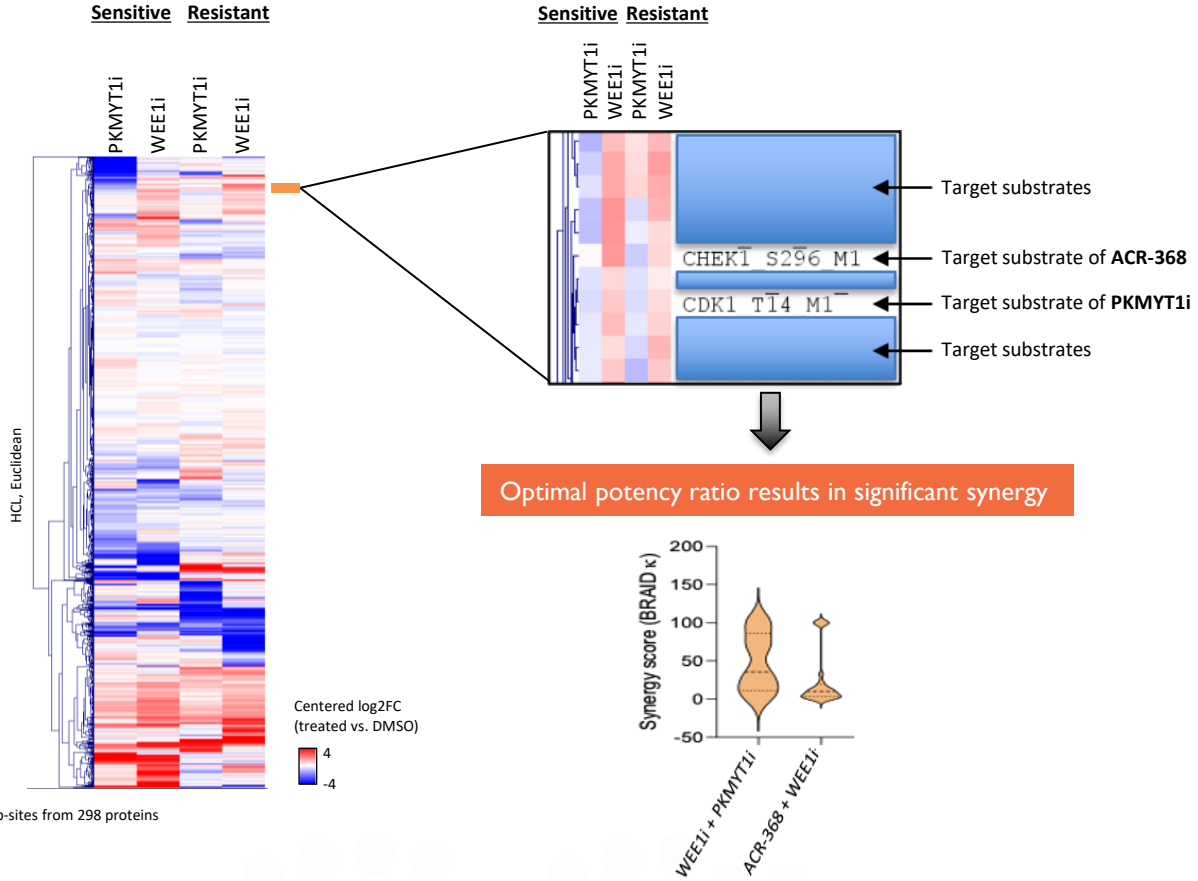


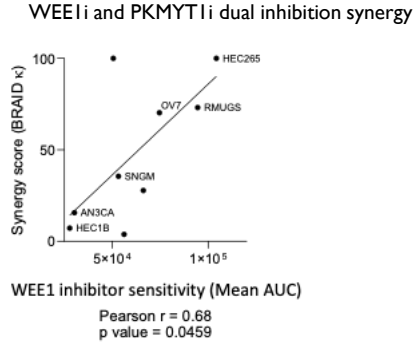
*Clinical-stage selective WEE1 and PKMYT1 inhibitors

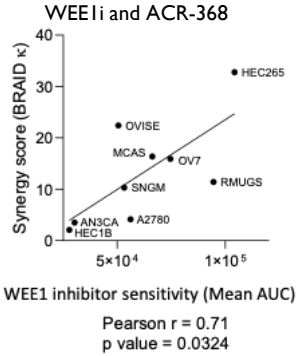
AP3-DERIVED DUAL POTENCY OPTIMIZATION TO OVERCOME WEE1 INHIBITOR RESISTANCE: RECIPROCAL QUENCHING



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







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

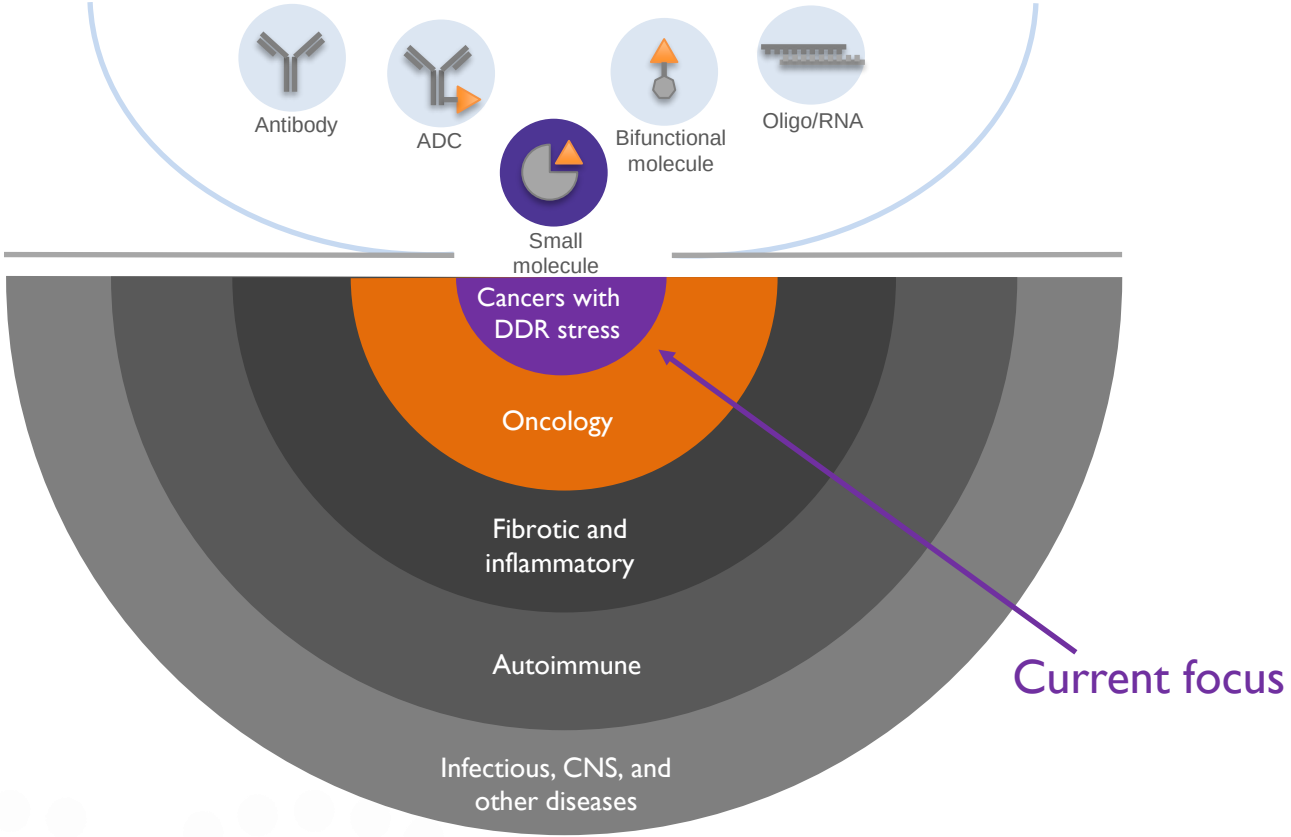
Streamlined Development

- Aiming for expedited monotherapy development
- Rapidly advancing towards IND in Q4 2024
- OncoSignature test in development for indication finding
- Dose optimization to be guided by drug target engagement (BM2)

THE AP3 APPROACH IS MODALITY AND DISEASE AGNOSTIC

Therapeutic modalities

Therapeutic areas



FINANCIAL HIGHLIGHTS

Cash and marketable securities

$127.5M

Balance sheet 31-Dec-2023

Projected runway into

Q4'25

Current operating plan, assuming no additional financing

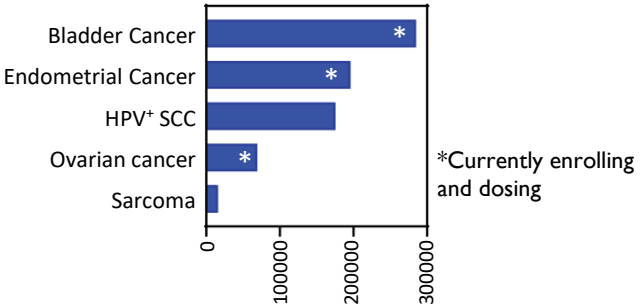
Fully Diluted Shares Outstanding

27.4M

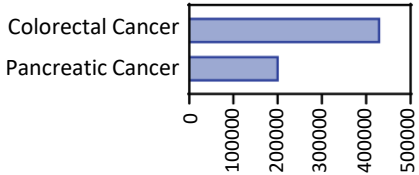
Shares and equity grants outstanding 31-Dec-2023

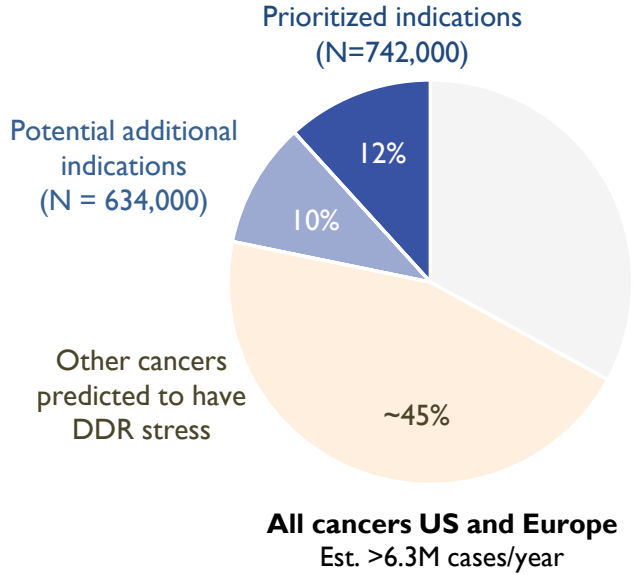
ACRIVON ADDRESSABLE MARKETS (US & EU INCIDENCE)

Prioritized indications for single agent ACR-368



Potential additional indications for single agent ACR-368





All cancers US and Europe
Est. >6.3M cases/year

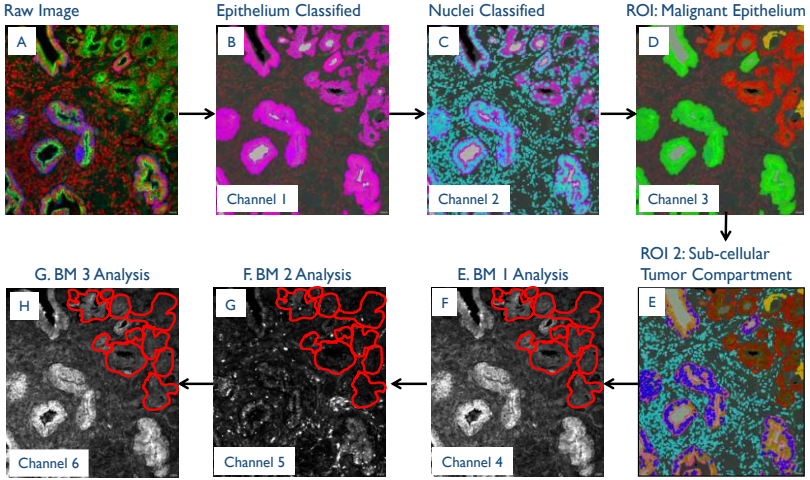
- ~30% (N = 223,000) of prioritized indications predicted sensitive to single agent ACR-368
- WEE1 and/or PKMYT1 inhibitor combinations with ACR-368 might further expand addressable fraction within sensitive tumor types

US cancer stats are based on ACS 2022 publication and subtype estimation from literature; EU cancer stats are based on IARC 2020 publication and subtype estimation from literature.
Cancers with DDR stress are estimated to be 67% which is calculated from MSK-IMPACT patient samples with DDR relevant mutations and CNVs, such as TP53, KRAS, CCNE1, etc.

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

Cell Reports (2018)

SHP2-i: SHP099 -allosteric inhibitor.

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

Cell Reports (2017)

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

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

Cell Reports (2017)

CDK7-i: THZ-1

Phosphoproteomics of Primary Cells Reveals Druggable Kinase Signatures in Ovarian Cancer

Cell Systems (2017)

Deepest proteome resolution of a human cell to date

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

Cell (2019)

Functional mapping of differential signaling by RPTK mutants

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

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

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

Nature Communications (2021)

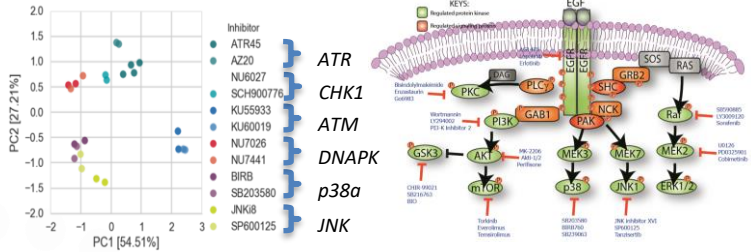
Clinically actionable resistance mechanisms

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

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



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

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

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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

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

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- Previously oncologist Royal Marsden, London and Inst. Cancer Res, London
- Lead/P.I. on numerous DDR trials

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

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

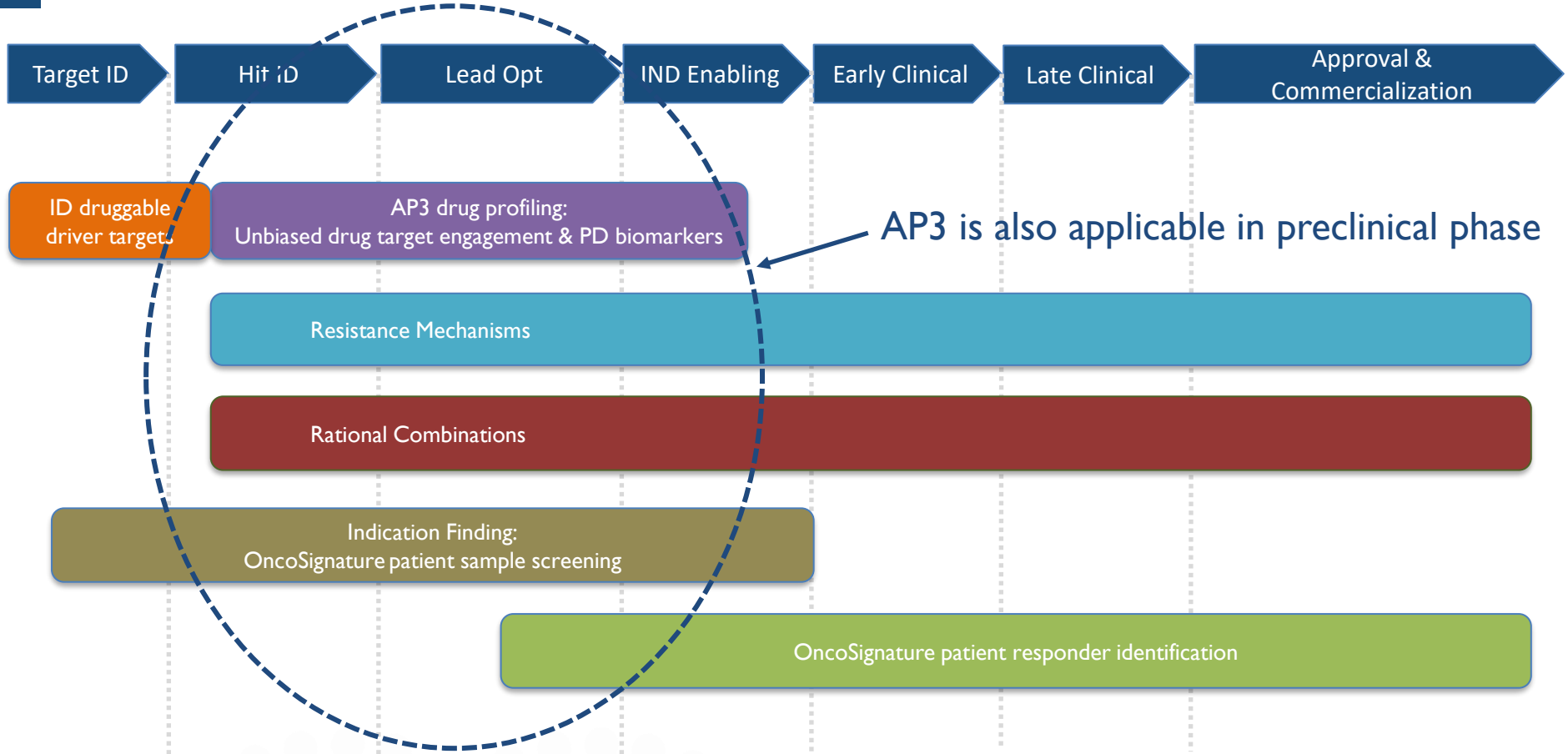
Jung-Min Lee, M.D.

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

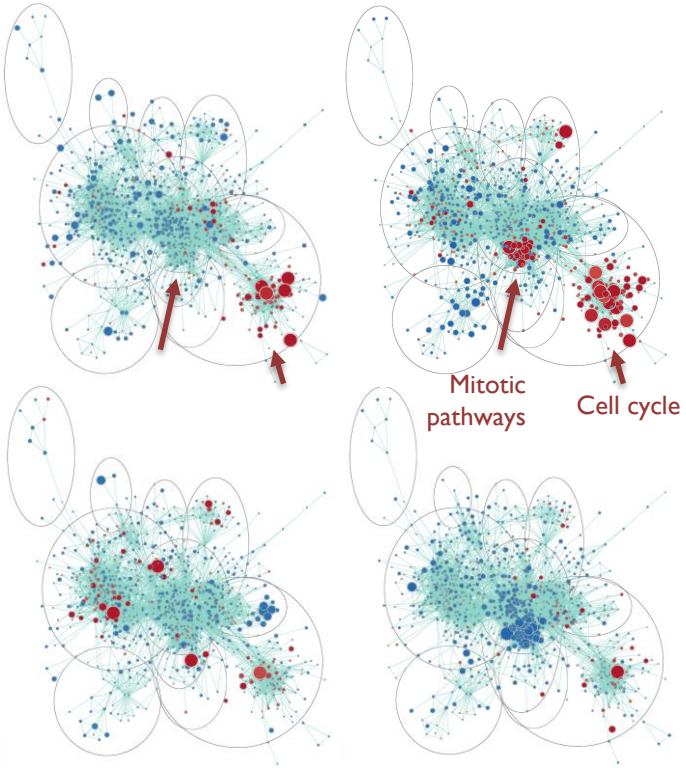
60min
200nM

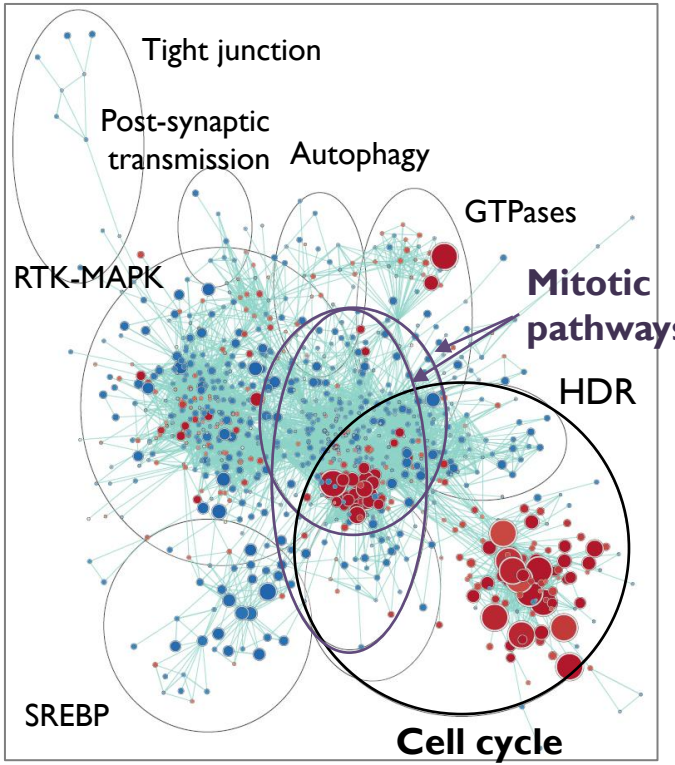
WEE1 inhibitor

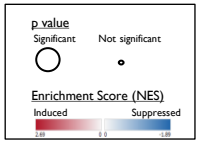
ACR-2316

Sensitive

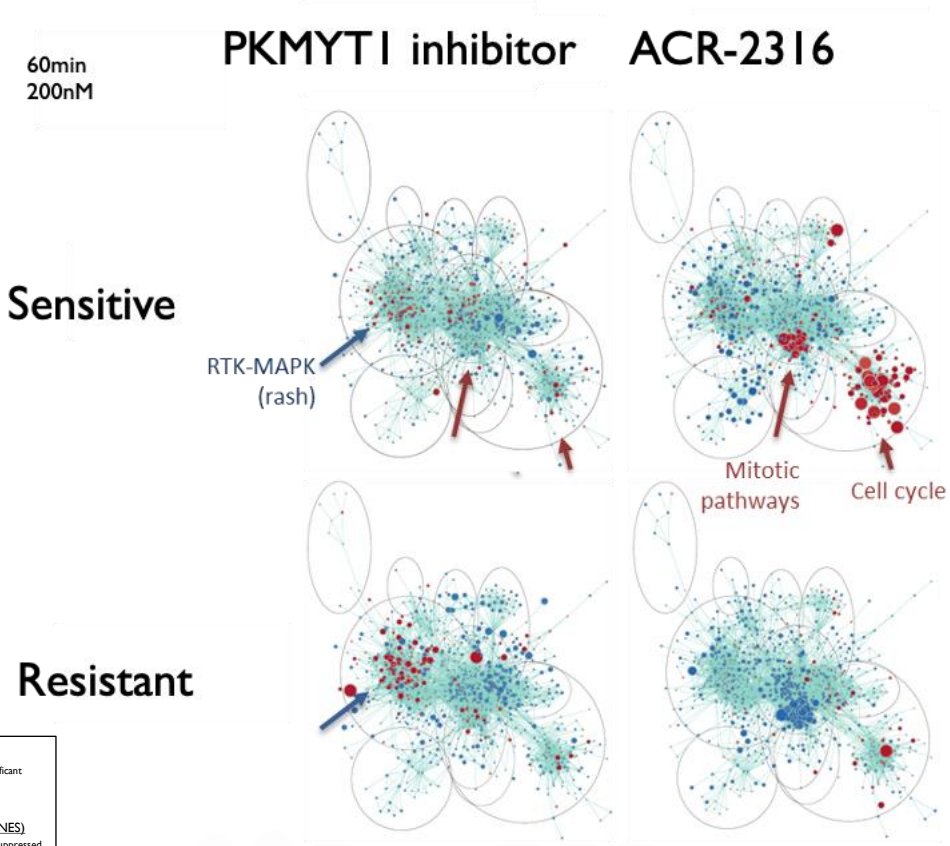
Resistant

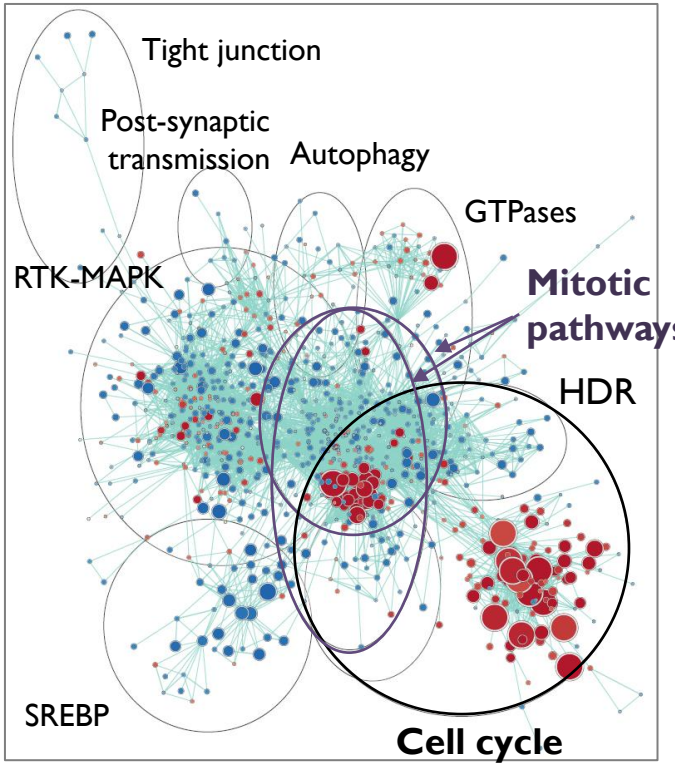






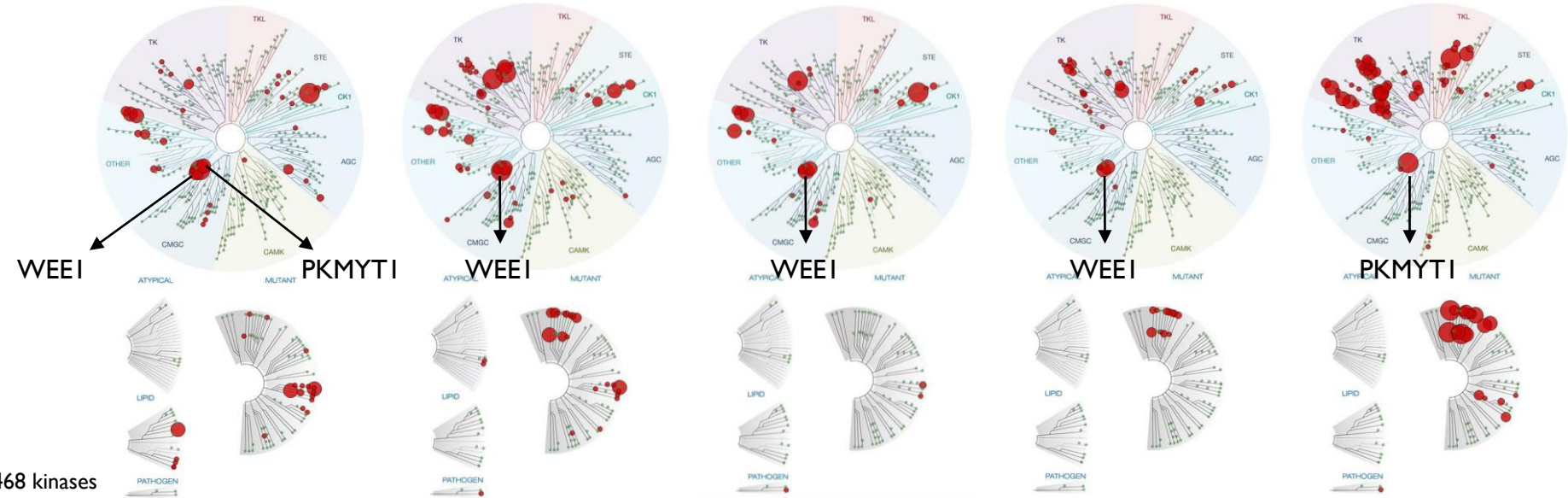
AP3 ANALYSIS: ACR-2316 REGULATES CELL CYCLE AND MITOSIS MORE POTENTLY THAN BENCHMARK PKMYT1 INHIBITOR





COMPREHENSIVE KINOME SELECTIVITY PROFILING

ACR-2316 | Adavosertib | Azenosertib | Debio0123 | Lunresertib



468 kinases
@ 1μM

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

KinomeScan

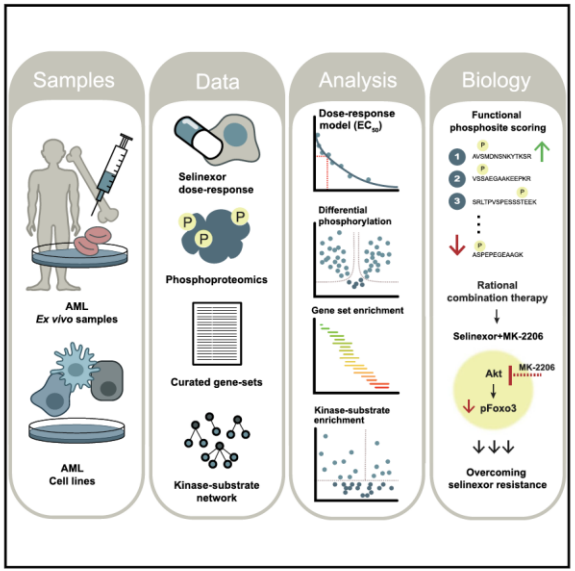
AP3 REVEALS SINGLE AGENT SENSITIVITY CONTEXT AND RATIONAL DRUG COMBINATIONS INDEPENDENT OF GENETIC INFORMATION

Article

Cell Reports

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

Graphical abstract



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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

- 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