UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 8, 2024

Acrivon Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-41551**	**82-5125532**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

480 Arsenal Way, Suite 100 **Watertown, Massachusetts** **(Address of Principal Executive Offices)**	**02472** **(Zip Code)**

(617) 207-8979
(Registrant's Telephone Number, Including Area Code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value	ACRV	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure

Beginning on January 8, 2023, Acrivon Therapeutics, Inc. (the "Company") will participate in the 42nd Annual J.P. Morgan Healthcare Conference. The Company has updated its corporate presentation that it intends to use in connection with its presentation on January 11, 2024 at 2:15 PM Eastern Time and in meetings with investors. The presentation includes, among other things, information on the development of the Company's product candidates and confirmation of its projected cash runway into the second half of 2025.

A copy of the Company's corporate presentation is attached hereto as Exhibit 99.1 and is hereby incorporated by reference herein.

The information furnished under Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1, is being furnished and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits:

Exhibit Number	Exhibit Description
99.1	Acrivon Therapeutics, Inc. Presentation
104	Cover Page Interactive Data File (formatted as Inline XBRL).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Acrivon Therapeutics, Inc.

Dated: January 8, 2024

By: /s/ Peter Blume-Jensen
Name: Peter Blume-Jensen, M.D., Ph.D.
Title: Chief Executive Officer and President

Exhibit 99.1

Acrivon Therapeutics

ACRIVON PREDICTIVE PRECISION PROTEOMICS (AP3)

OVERCOMING LIMITATIONS OF GENETICS-BASED PRECISION MEDICINE

CORPORATE PRESENTATION

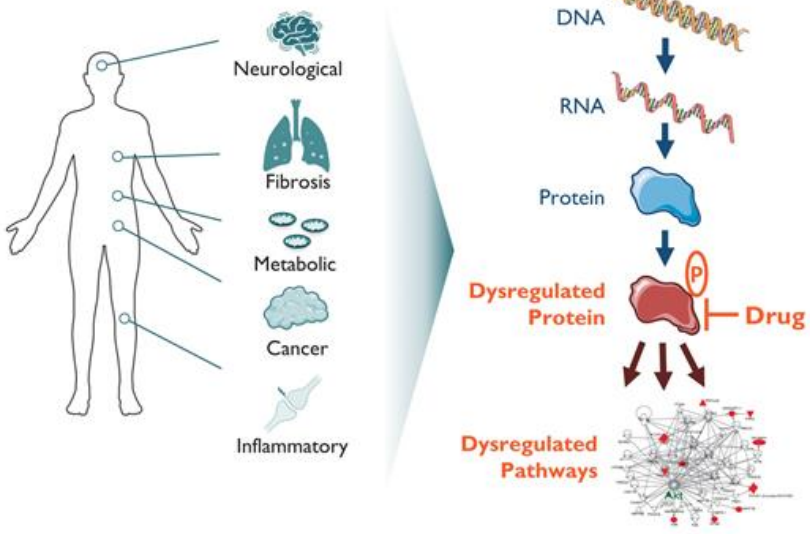
JANUARY 2024

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.

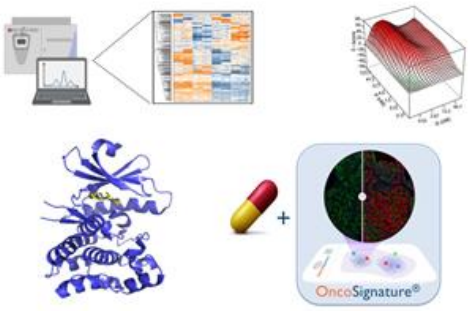
You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this presentation. We undertake no obligation to update any forward-looking statements or to reflect new information or the occurrence of unanticipated events, except as required by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

ACRIVON THERAPEUTICS – A NEXT-GENERATION PRECISION MEDICINE COMPANY

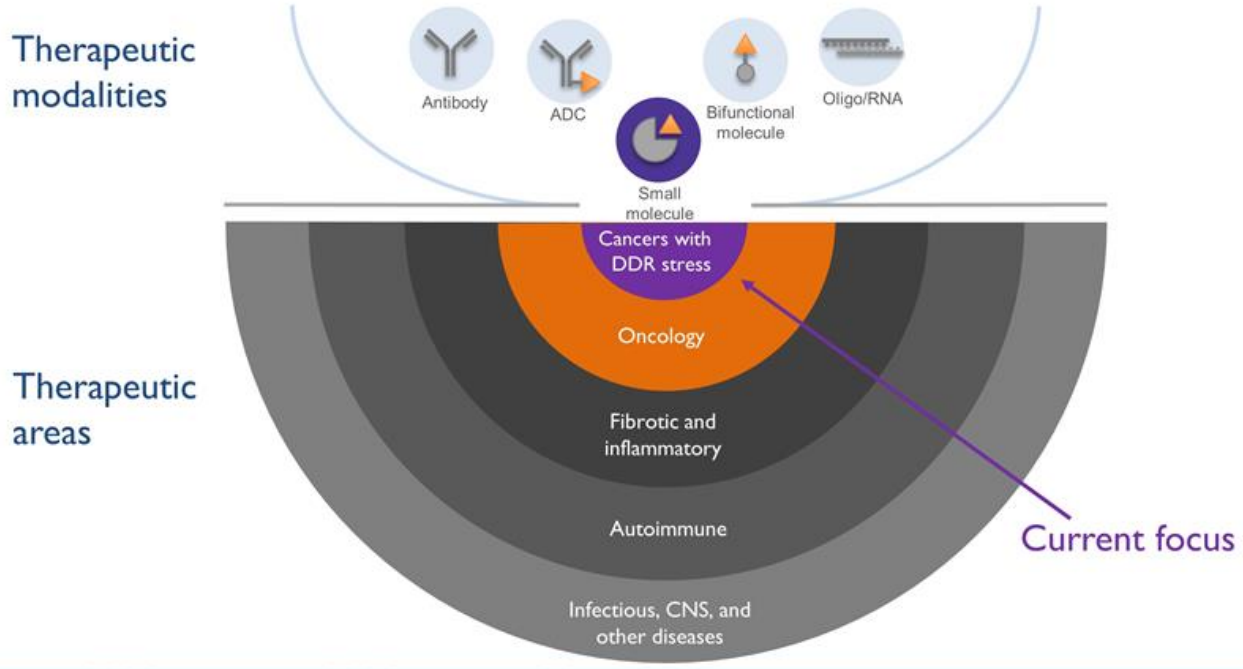


Acrivon Predictive Precision Proteomics (AP3)

- Enables an exact match between the disease-causing, dysregulated pathways with a drug's mechanism of action (Acrivon meaning ≈ exact, accurate)
- Is broadly applicable in drug discovery and development (including SAR and optimal selectivity, uncovering resistance mechanisms, and patient responder identification) and being leveraged for our internal therapeutics pipeline



THE AP3 APPROACH IS MODALITY AND DISEASE AGNOSTIC



ACRIVON: NEXT GENERATION PRECISION ONCOLOGY

OVERCOMING LIMITATIONS OF GENETICS-BASED PRECISION MEDICINE

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

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
- 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"

ACRIVON THERAPEUTICS AT A GLANCE

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

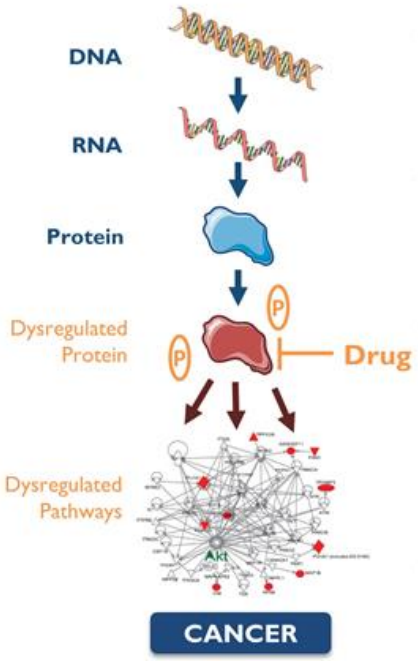
Jesper V. Olsen
Academic Co-Founder. Novo-Nordisk Foundation Protein Center, Cph.

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

ACRIVON PREDICTIVE PRECISION PROTEOMICS, AP3



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

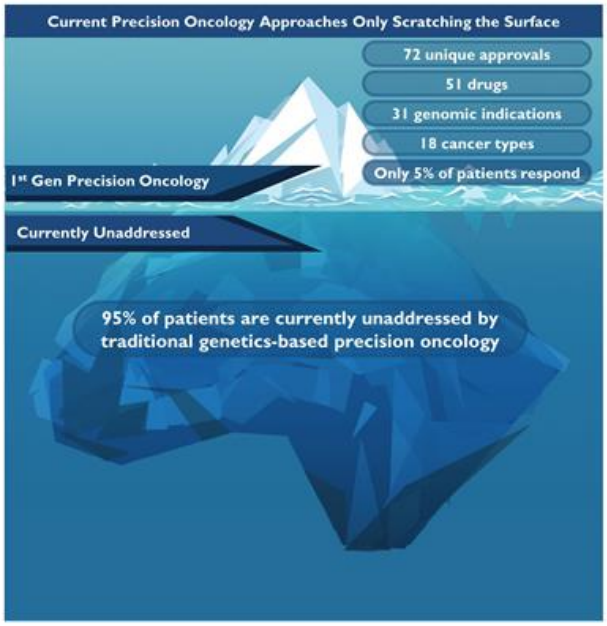
CANCER IS CAUSED BY DYSREGULATED PROTEIN ACTIVITY

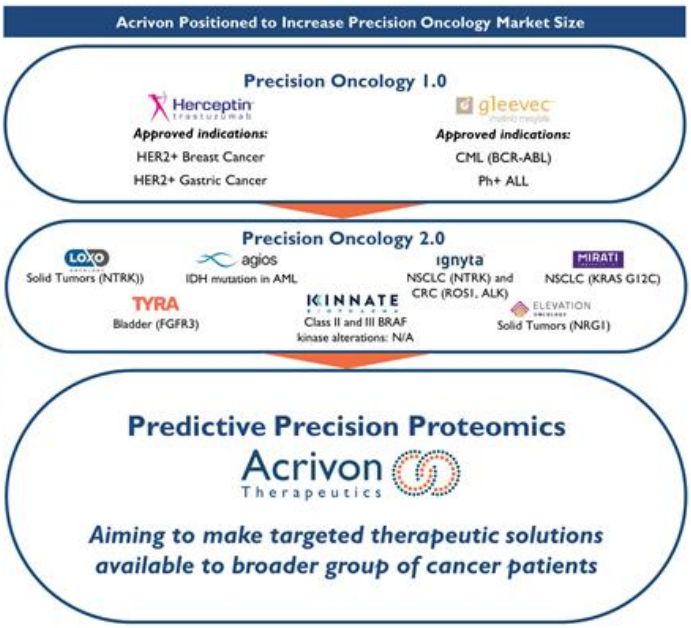
Acrivon's AP3 platform directly measure the disease-driving, dysregulated proteins and is designed to enable an exact match with the drug mechanism-of-action independent of genetic alterations

(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)

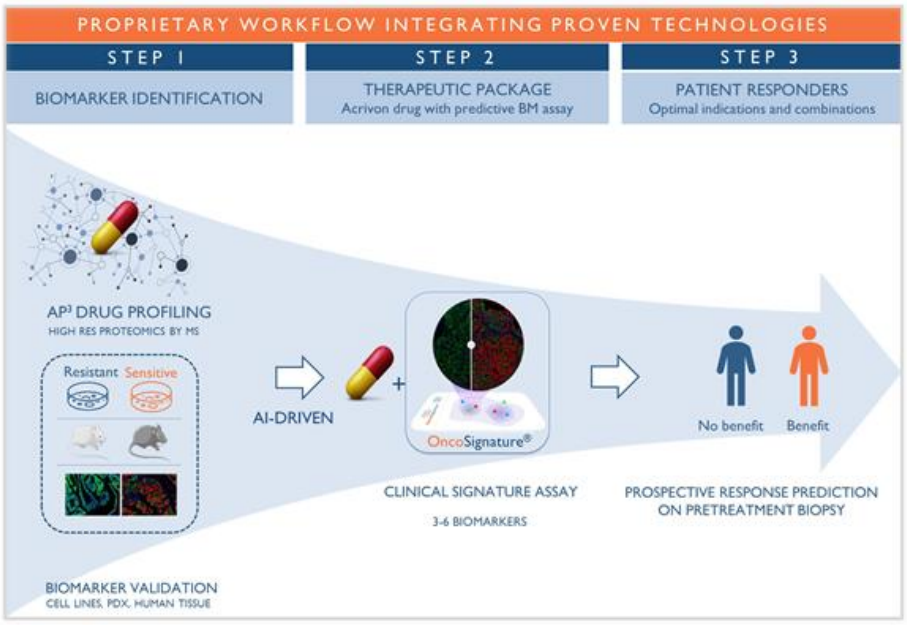
AP3 PLATFORM ADDRESSES HIGH UNMET NEED BEYOND NGS-BASED PRECISION MEDICINE

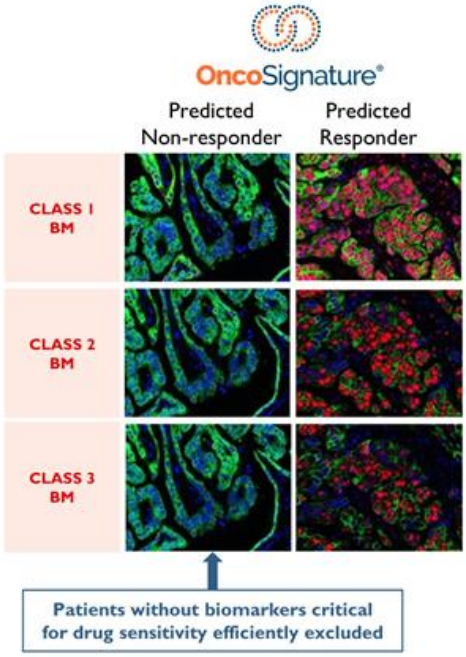




Sources: Company Filings, ACS, CDC, NCI, Wall Street Research (2022)

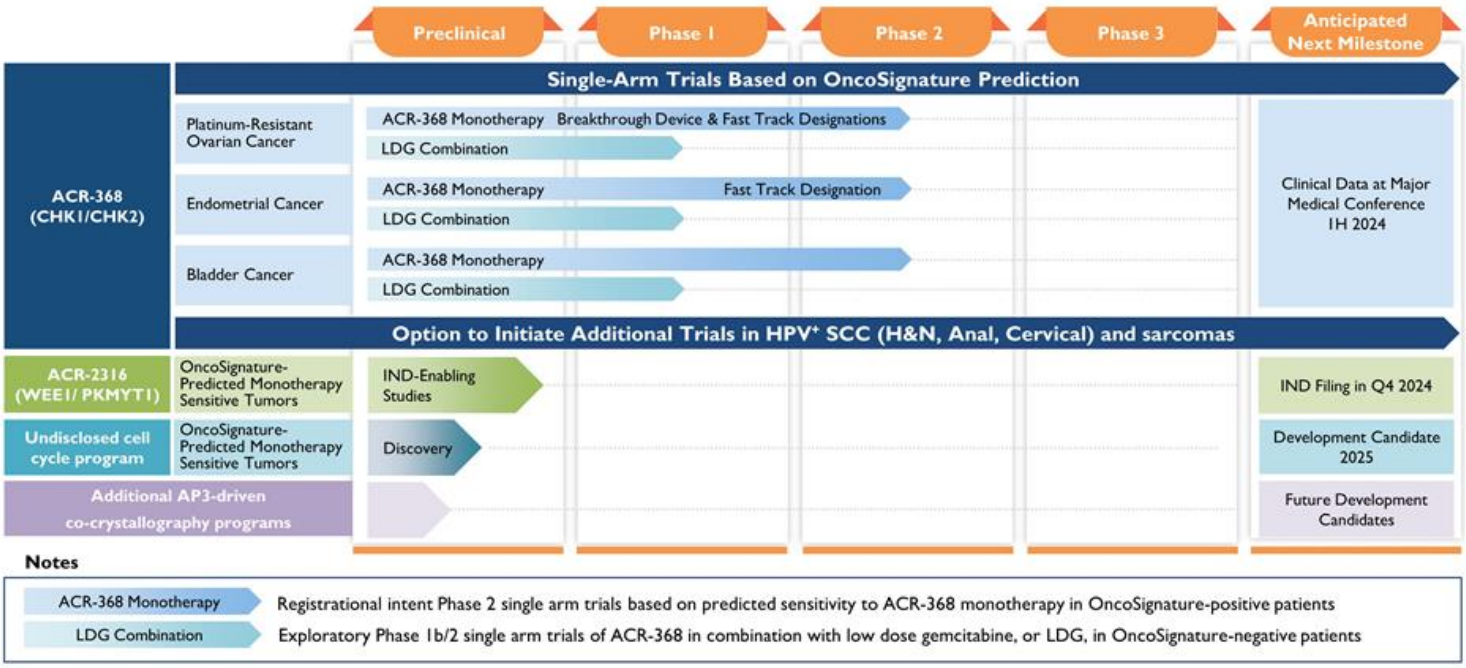
AP3 PLATFORM: DRUG RESPONSE PREDICTION IN INDIVIDUAL PATIENTS





"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

ACRIVON PIPELINE

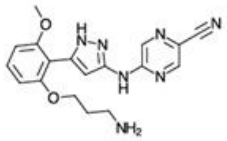


Notes

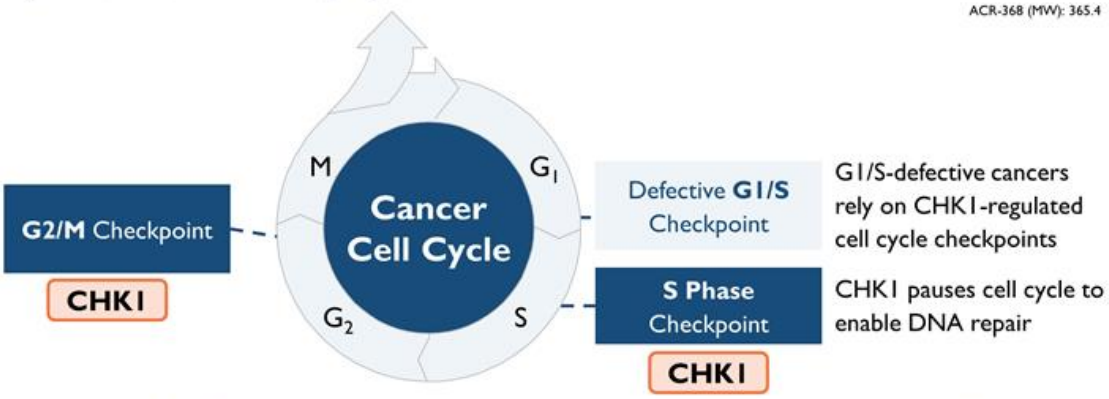
ACR-368 Monotherapy	Registrational intent Phase 2 single arm trials based on predicted sensitivity to ACR-368 monotherapy in OncoSignature-positive patients
LDG Combination	Exploratory Phase 1b/2 single arm trials of ACR-368 in combination with low dose gemcitabine, or LDG, in OncoSignature-negative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

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

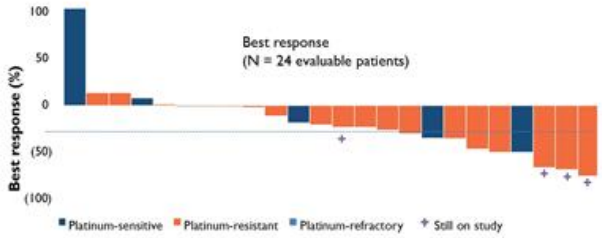
PAST PHASE 2 TRIALS IN HIGH GRADE SEROUS OVARIAN CANCER

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

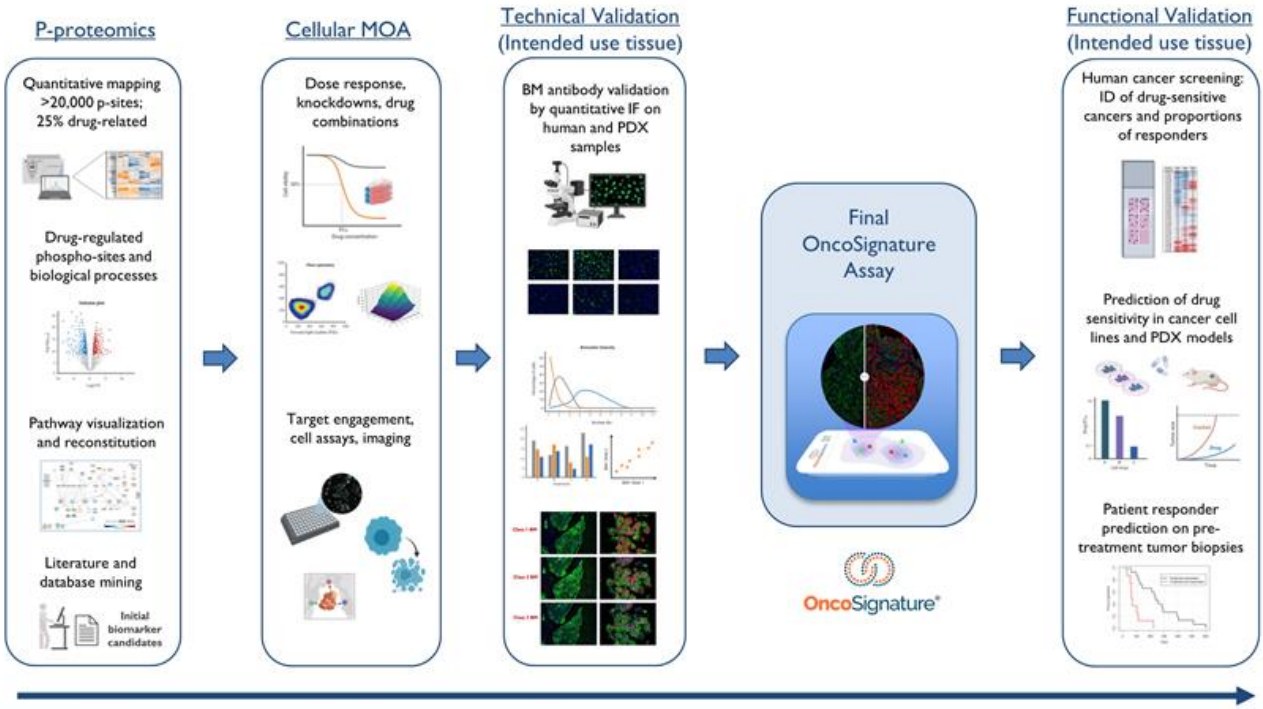
- ORR 12.1% (excl. unconfirmed); mDoR =5.6 months
- No correlation with genetic alterations

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

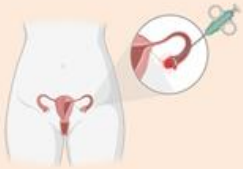
- ✓ Past trials suggest unenriched all-comer ORR in HGS ovarian cancer is ~15-20%
- ✓ Durable clinical activity in most responders
- ✓ No predictive biomarkers identified, need for alternative biomarker approach (ideal for AP3)

DEVELOPMENT OF AP3-BASED PATIENT SELECTION ONCOSIGNATURE TESTS



ONCOSIGNATURE TESTS: USAGE IN THE CLINIC

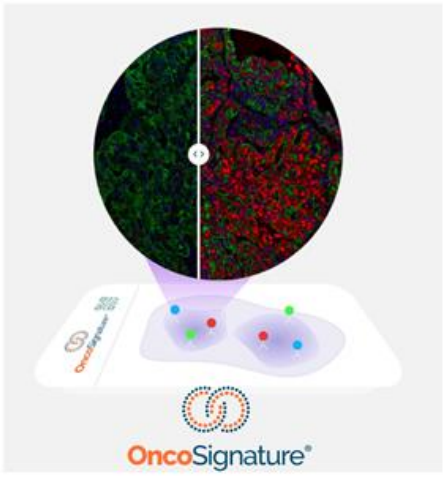
Pretreatment tumor biopsy



Sample processing

Biopsy in FFPE block

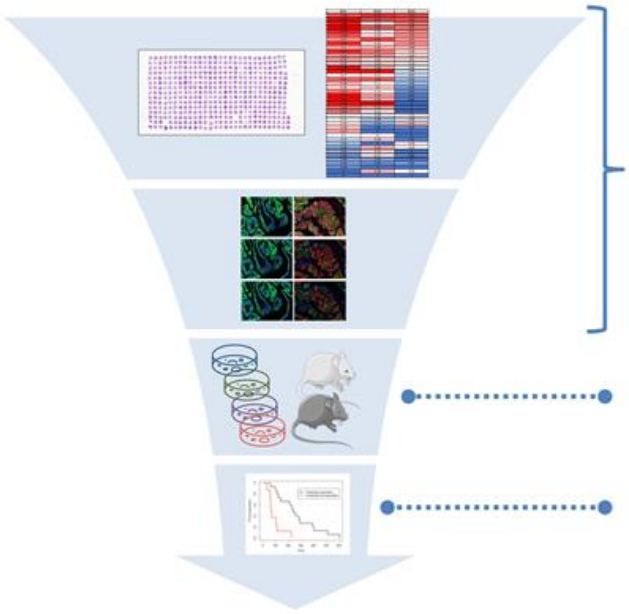
Automated tumor Region-of-Interest biomarker scoring



- 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

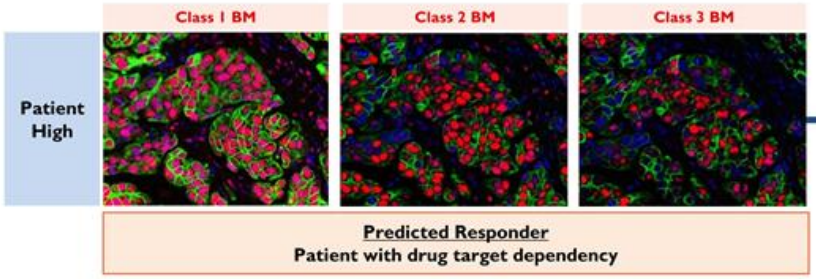
CONSISTENT ACR-368 ONCOSIGNATURE PERFORMANCE ACROSS PRECLINICAL STUDIES



OncoSignature®

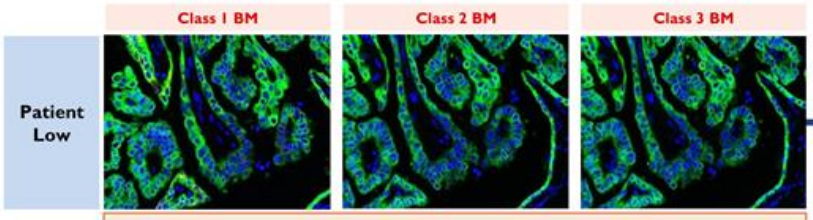
- Prediction of the fraction of human tumors sensitive to single agent ACR-368
  - Selection rate 30-40% across lead indications
- Identification of additional human tumor types predicted sensitive to single agent ACR-368
  - Endometrial and bladder cancer
- Prediction of treatment outcome in human PDX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

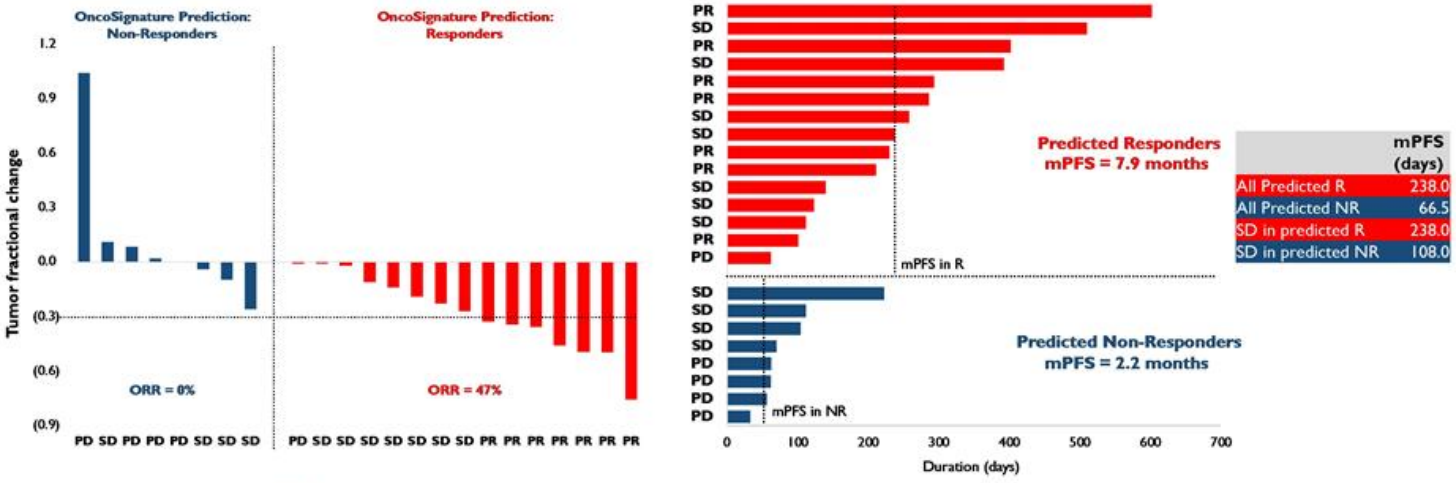


Predicted Non-Responder
Patient with no drug target dependency efficiently excluded

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



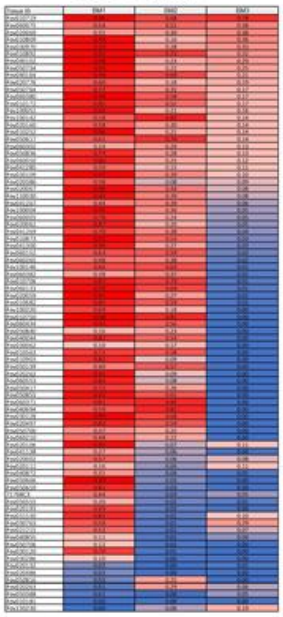
	mPFS (days)
All Predicted R	238.0
All Predicted NR	66.5
SD in predicted R	238.0
SD in predicted NR	108.0

OncoSignature®

Result: ORR ~47%; mPFS = 7.9 months

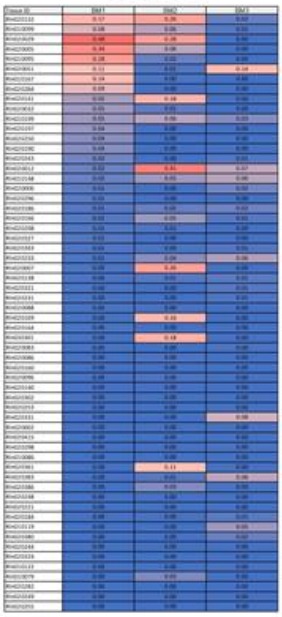
TWO ADDITIONAL HIGH UNMET NEED SOLID CANCERS PREDICTED ACR-368-SENSITIVE THROUGH HUMAN TUMOR SAMPLE SCREENING

HGS Ovarian



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

Sq. NSCLC



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

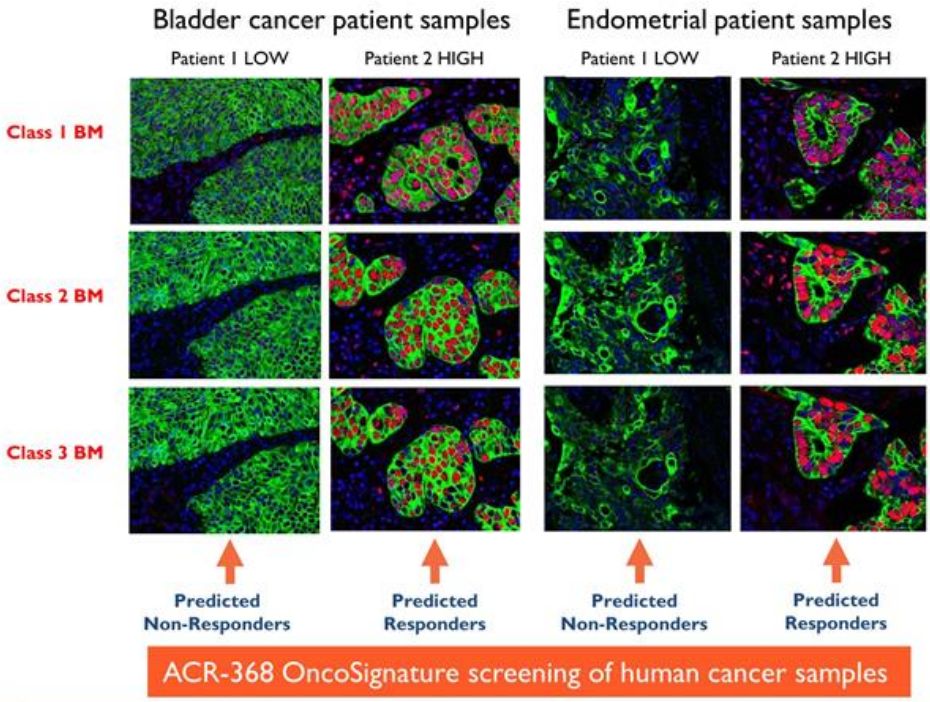
Bladder cancer

OncoSignature-positive = 30-50%

Endometrial cancer

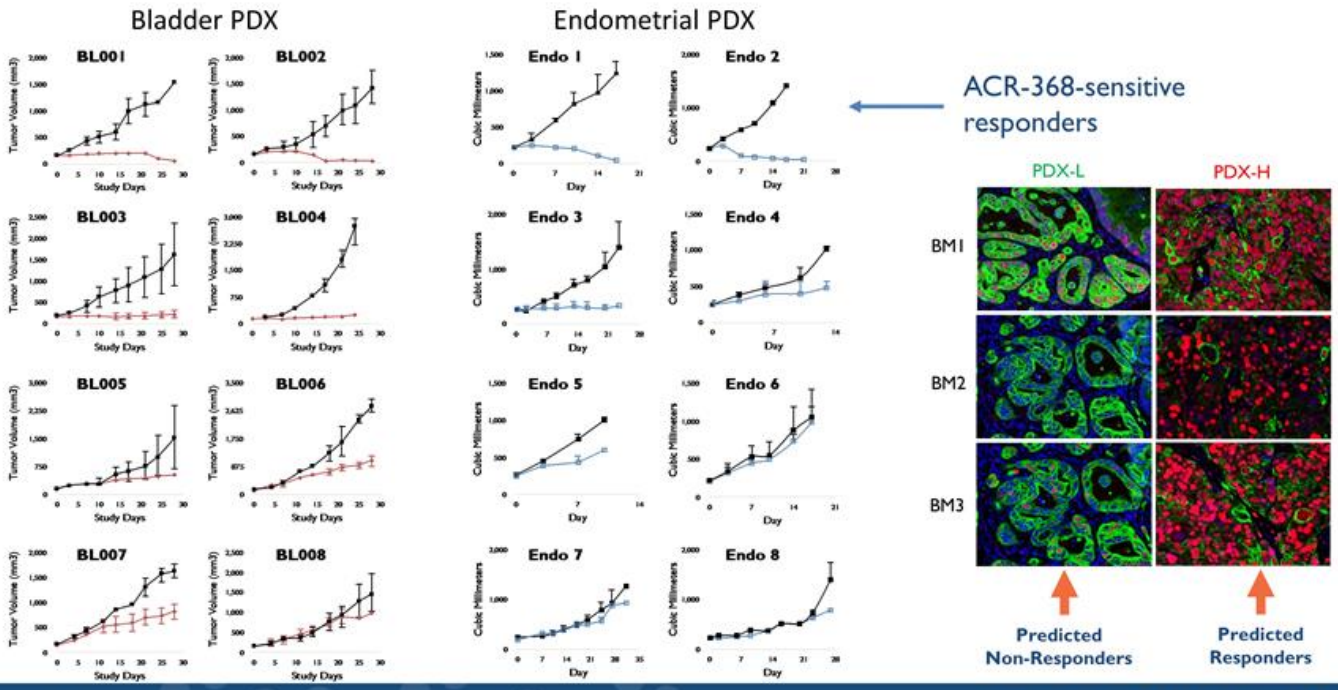
OncoSignature-positive = 30-40%

TWO ATTRACTIVE ACR-368-SENSITIVE CANCER TYPES IDENTIFIED

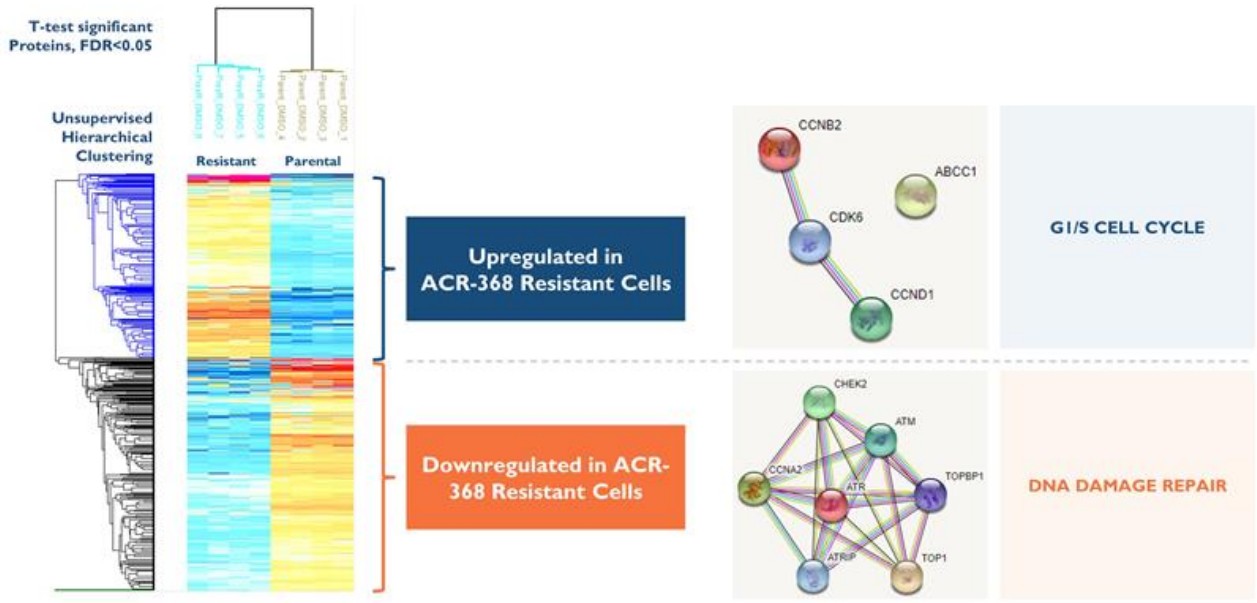


ACR-368 OncoSignature screening of human cancer samples

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

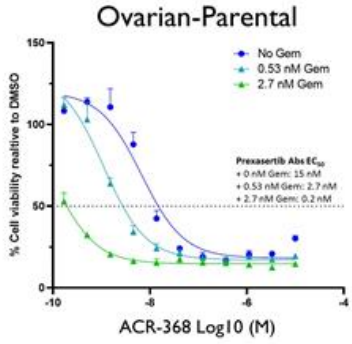


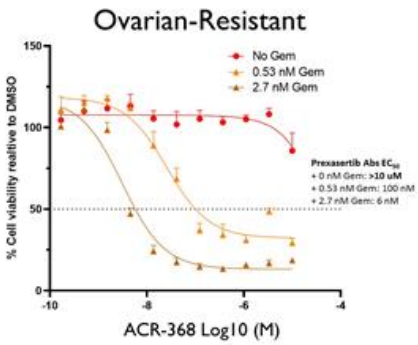
AP3 UNCOVERS ACTIONABLE ACR-368 RESISTANCE MECHANISMS UNBIASED AND INDEPENDENT OF GENETIC INFORMATION

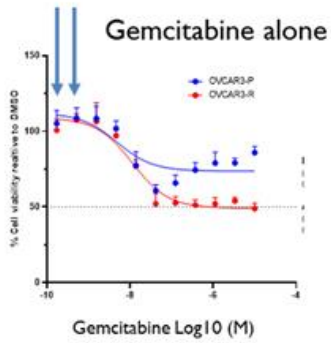


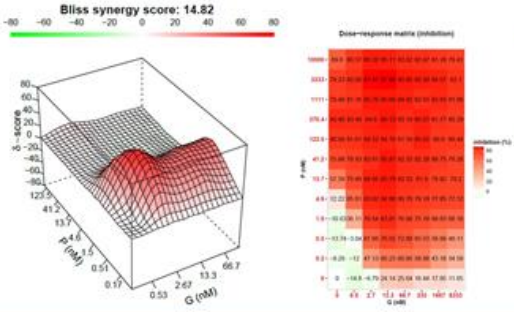
Data suggest that gemcitabine might be a rational combination to overcome DDR suppression

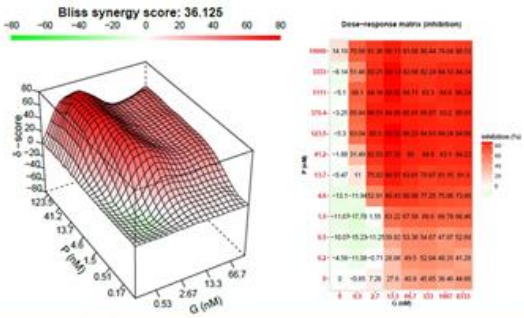
LOW DOSE GEMCITABINE SENSITIZES OVARIAN CANCER CELL LINES TO ACR-368









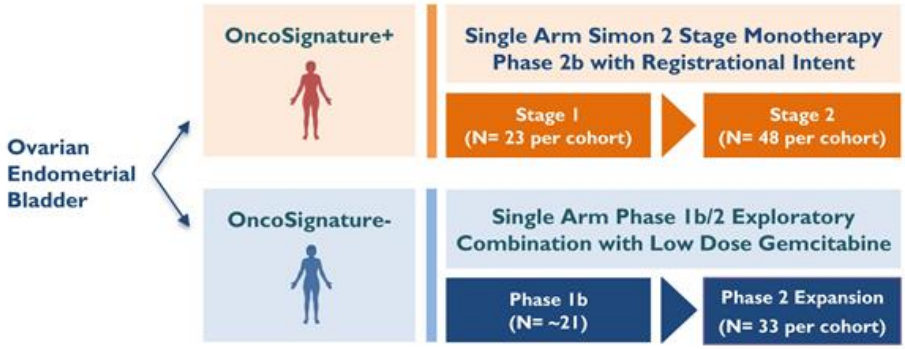


Bliss Synergy score:

- <-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
- 59 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

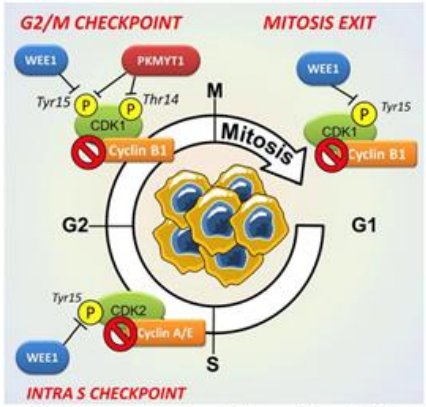
ENCOURAGING INITIAL CLINICAL OBSERVATIONS

- 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

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 through phosphorylation and inhibition of CDK2 and CDK1 and CDK1, respectively
- 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:
  - Adavosertib (AstraZeneca)
  - Debio0123 (Debiopharm)
  - Azenosertib (Zentalis Pharmaceuticals)
  - SGR-3515 (preclinical, Schrödinger)
  - Lunresertib (Repare Therapeutics)



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

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

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

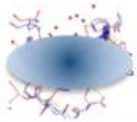
Rationale

- *Leveraging our AP3 patient selection platform for high clinical POS*
- *Potentially optimal profile for monotherapy clinical development*

ACR-2316 and other DDR programs

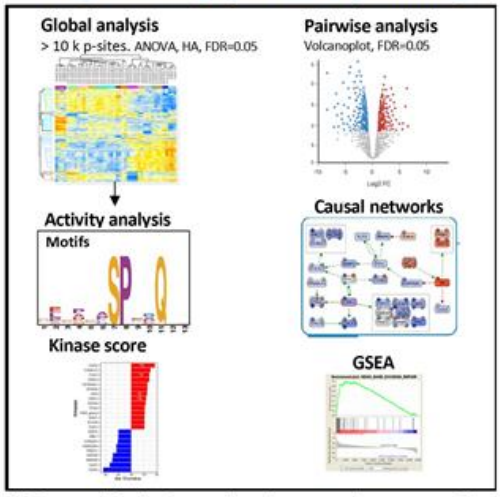
- >40 high resolution co-crystals (1.5-3.1 Å) and AP3-driven SAR
- Novel WEE1- and PKMYT1-selective structural series and lead candidates
- Optimal selectivity profiles generated based on AP3 profiling

ACR-2316 advancing in IND-enabling studies



- High resolution co-crystals with WEE1 and PKMYT1
- Novel, potent dual inhibitor (single digit nM potency)
- Designed to overcome WEE1 and PKMYT1 single inhibitor resistance
- Potent, selective single agent activity

High throughput AP3 profiling



AP3 used for biologically relevant selectivity profiling

EXECUTIVE SUMMARY: ACR-2316 DEVELOPMENT CANDIDATE

A selective dual WEE1/ PKMYT1 inhibitor optimized using AP3 for potent single agent activity

On track for IND by Q4 2024 preparing for monotherapy clinical development

AP3-Enabled Differentiation

- Discovered by AP3-based SAR facilitated by co-crystallography with WEE1 and PKMYT1
- Unbiased detection of WEE1 inhibitor-induced resistance mechanisms, overcome by balanced PKMYT1 inhibition to achieve potent single agent activity
- ACR-2316 OncoSignature test being developed for indication finding and monotherapy clinical development

Mechanism of Action

- Single digit nM WEE1 inhibition with optimized ratio of PKMYT1 inhibition in cells
- Superior selectivity and potency compared to clinical benchmark WEE1 and PKMYT1 inhibitors
- Potent induction of CDK1/2 and PLK activity resulting in drastic induction of mitotic catastrophe

Preclinical Data

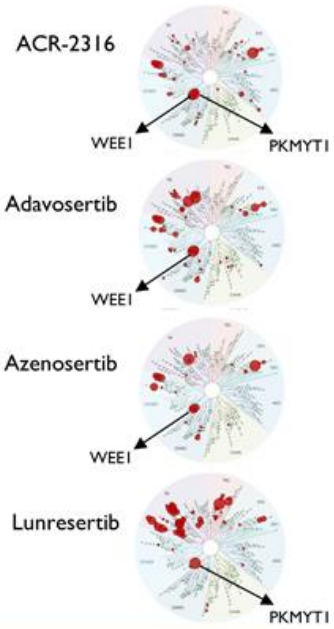
- Superior activity across human tumor cell lines and in mouse tumor models, vs clinical benchmark WEE1 and PKMYT1 inhibitors
- Favorable in vitro ADME, PK, and oral bioavailability with safety MTD/DRF studies consistent with predicted desirable human exposure
- Advancing rapidly in ongoing IND-enabling studies

ACR-2316 SHOWS ATTRACTIVE PROFILE IN ONGOING PRECLINICAL STUDIES

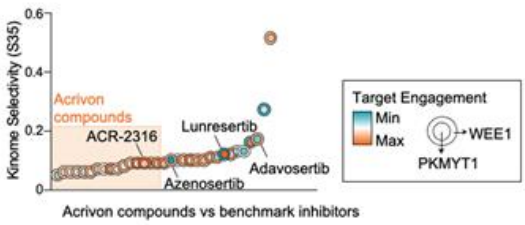
Relative performance	WEE1 cellular drug target engagement	PKMYT1 cellular drug target engagement	Kinome selectivity	Human tumor cell viability	In vivo efficacy
ACR-2316	**++++**	**++**	**++++**	**++++**	**++++**
Adavosertib	++	-	++	+++	++
Azenosertib	++	-	+++	++	++
Debio0123	+	-	++++	+	+
Lunresertib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

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

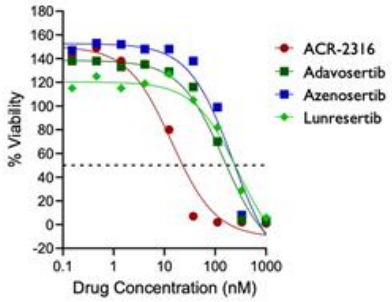
KinomeScan (468 kinases @ 1μM)



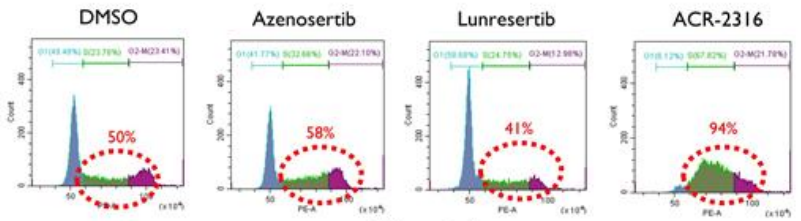
ACR-2316 is highly selective (KinomeScan)



ACR-2316 potently inhibits cancer cell viability



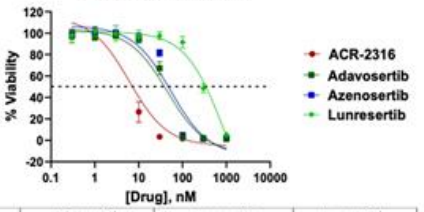
ACR-2316 exerts potent cell cycle effects with pronounced S-G2/M accumulation



100 nM, 24 hour

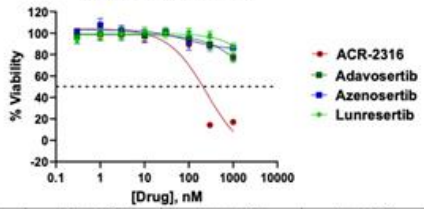
ACR-2316 SHOWS SUPERIOR ACTIVITY VS BENCHMARKS ACROSS ALL HUMAN TUMOR CELL LINES TESTED

Human Tumor Cell Line 1



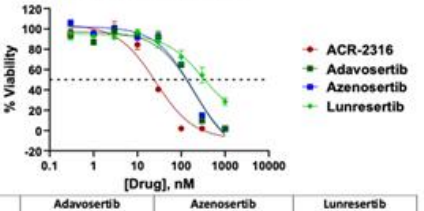
ACR-2316 IC50 (nM)	Adavosertib IC50 (nM)	Azenosertib IC50 (nM)	Lunresertib IC50 (nM)
7	39	47	340

Human Tumor Cell Line 2



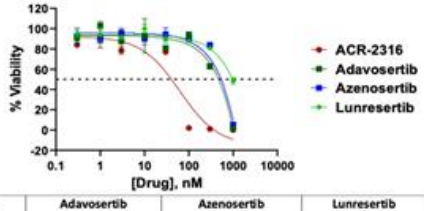
ACR-2316 IC50 (nM)	Adavosertib IC50 (nM)	Azenosertib IC50 (nM)	Lunresertib IC50 (nM)
207	> 1000	> 1000	> 1000

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



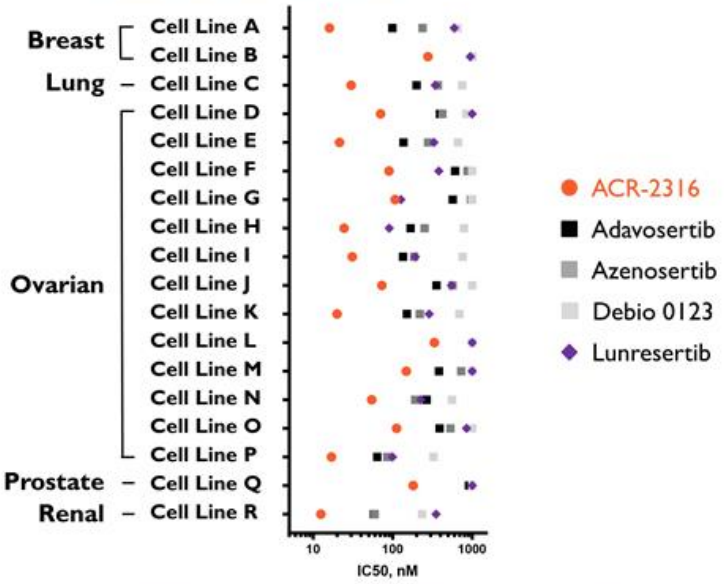
ACR-2316 IC50 (nM)	Adavosertib IC50 (nM)	Azenosertib IC50 (nM)	Lunresertib IC50 (nM)
40	471	533	967

Example: Ovarian human cancer cell lines

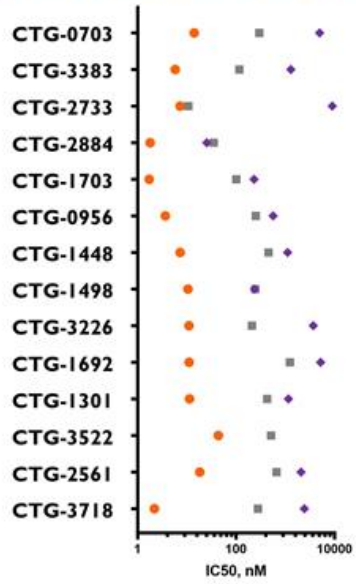
19 ovarian and other human tumor cell lines tested to date

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

Human tumor cell lines

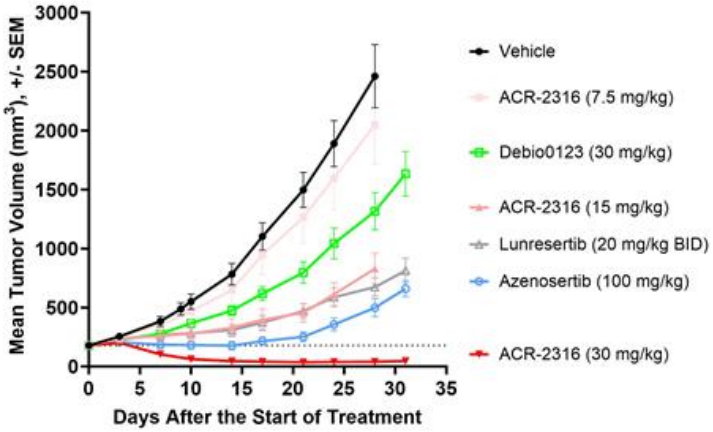


Patient-derived *ex vivo* tumor models

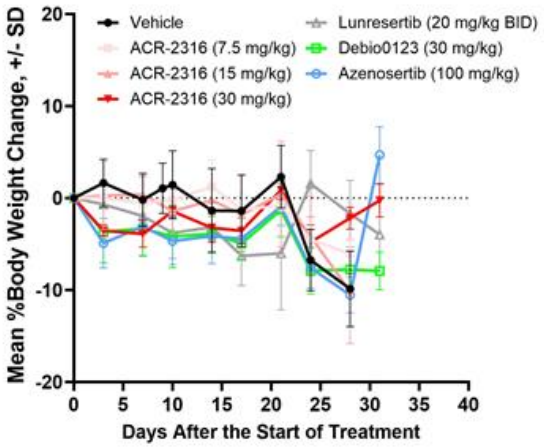


ACR-2316 SHOWS POTENT ANTI-TUMOR ACTIVITY COMPARED TO CLINICAL WEE1 OR PKMYT1 INHIBITORS

Efficacy (5 ON / 2 OFF)

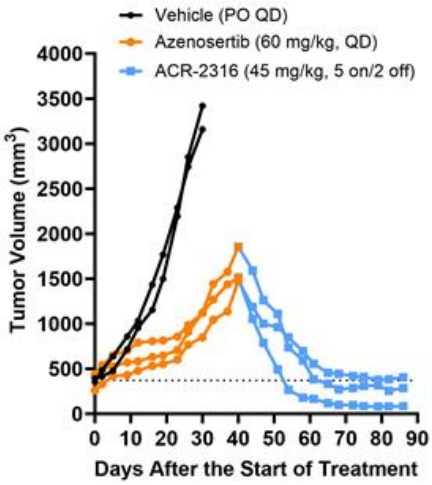


Tolerability (5 ON / 2 OFF)

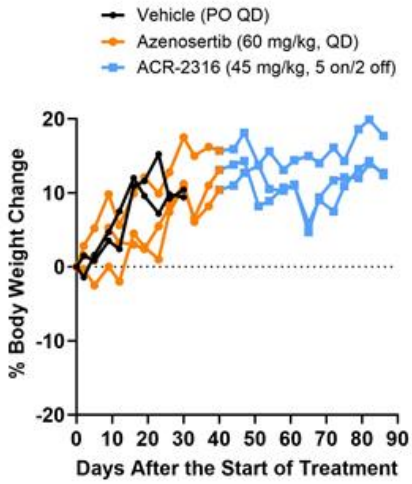


ACR-2316 SHOWS DEEP REGRESSION IN TUMORS PROGRESSING ON A BENCHMARK WEE1 INHIBITOR

Anti-tumor activity



Tolerability



ACR-2316 EMERGING SAFETY PROFILE FROM PRECLINICAL ANIMAL STUDIES APPEARS PROMISING

Mice:

- ACR-2316 is well-tolerated at target doses up to ≤60 mg/kg daily oral dosing resulting in tumor regression in xenograft mouse models
- Reversible, mechanism-based hematological effects; moderate reticulopenia, monocytopenia, and lymphopenia based on initial studies

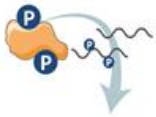
Rat and dog MTD and preliminary DRF studies:

- Plasma PK exposure consistent with projected human exposure levels required for potential anti-tumor activity
- Reversible, mechanism-based hematological effects (white blood cells)
- Primary toxicities at MTD were decreased activity, food consumption, and soft stool

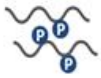
STREAMLINED AP3-BASED BIOLOGICAL SAR OPTIMIZATION FOR SINGLE AGENT ACTIVITY OF PRECLINICAL PROGRAMS

Drug treatment

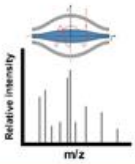
Proteolysis
P-peptide enrichment



Peptide clean up



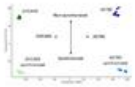
Ultra high resolution
P-proteomic profiling



Direct DIA analysis

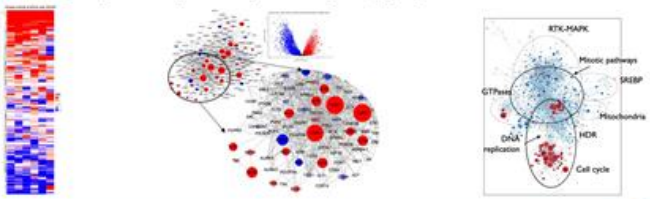
High resolution and throughput MS-based P-proteomics

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

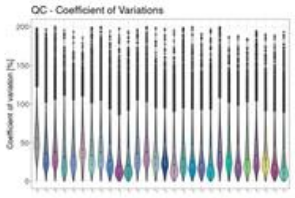
Week2

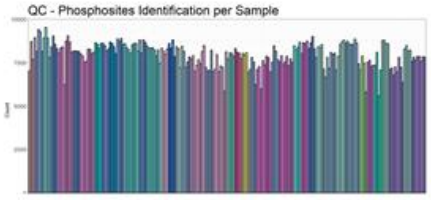
AP3: TIGHT, HIGH-RESOLUTION DATA WITH DEEP COVERAGE

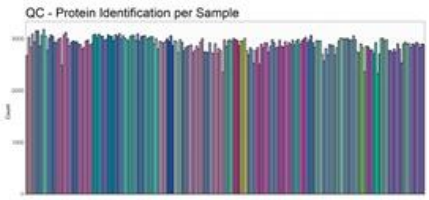
35388 p-sites

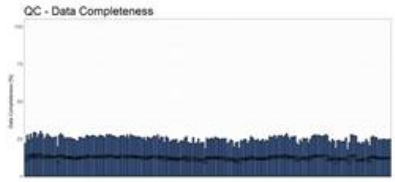
15733 p-sites

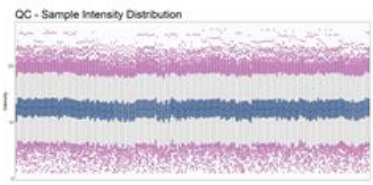
QC MS Data → Data Clean Up → QC Processed Data → Volcano Plots → Hierarchical Clustering → Consensus Sequence Motif → Kinase Inference → Pathway Enrichment → Functional Annotation → Network Mapping → Biomarkers

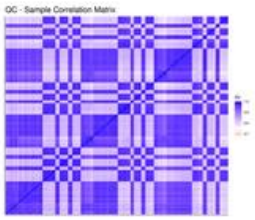






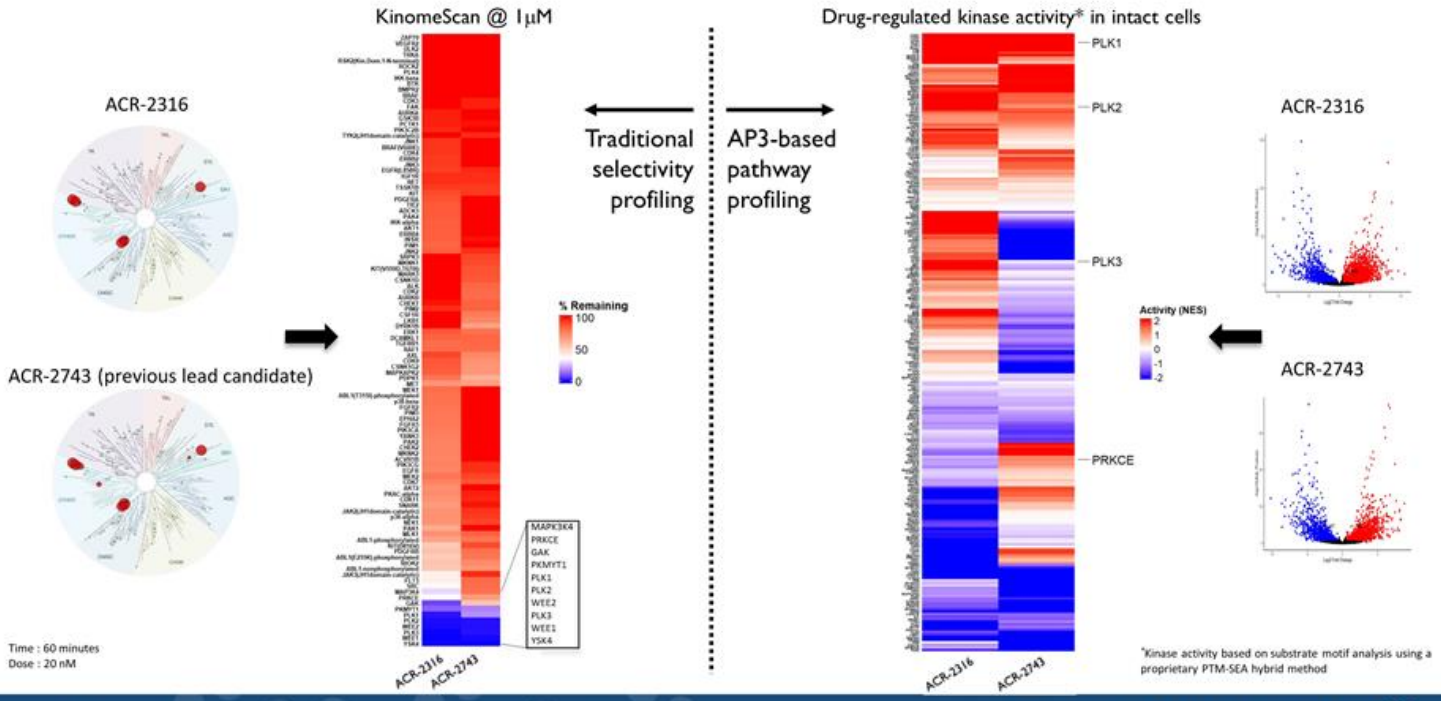






- ✓ Acrivon proprietary compound data (~30 million data points per experiment); dozens of compounds profiled
- ✓ Miniaturized, high throughput, scalable: <2 weeks turn-around, automated AI computational analyses in 1 day
- ✓ Actionable results: Resistance mechanisms, rational combinations, drug-tailored OncoSignature patient selection

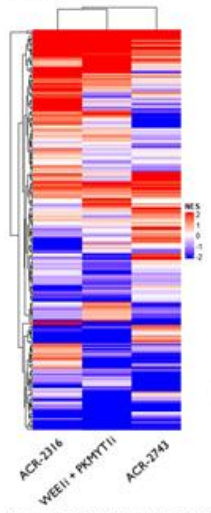
AP3 REVEALS DRUG-REGULATED KINASE ACTIVITY IN INTACT CELLS NOT DETECTABLE BY STANDARD METHODS



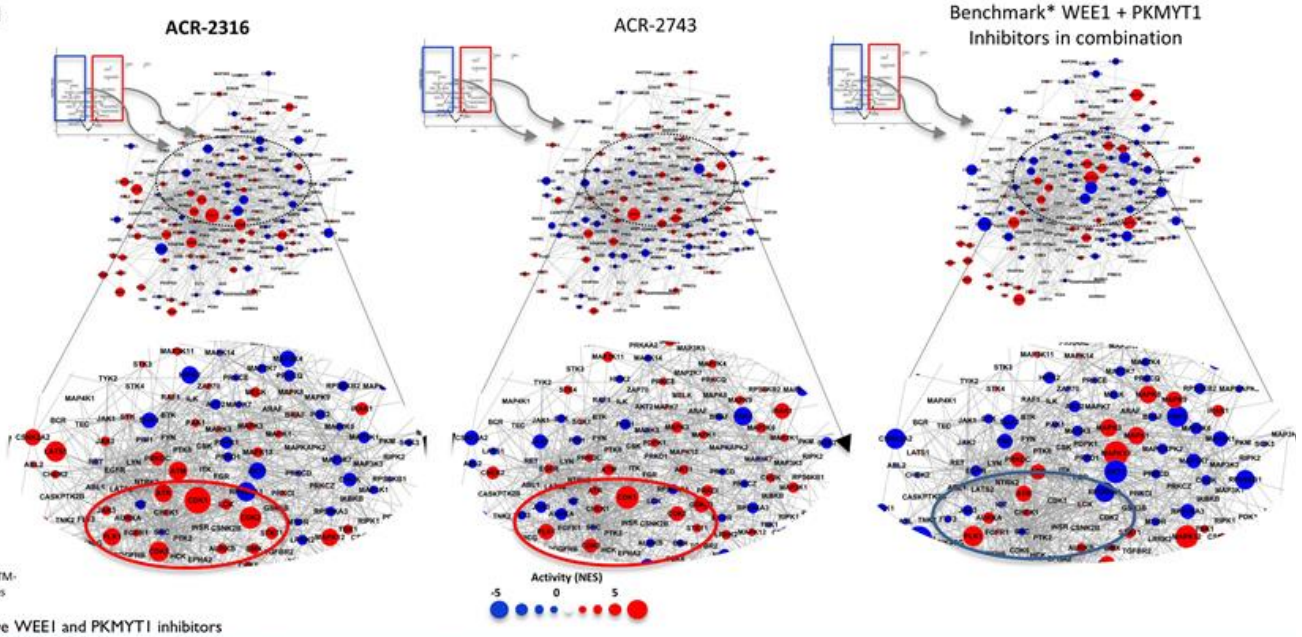
OPTIMIZED DUAL INHIBITORS SHOW DESIRABLE PATHWAY EFFECTS

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

Substrate motif-inferred kinase activities

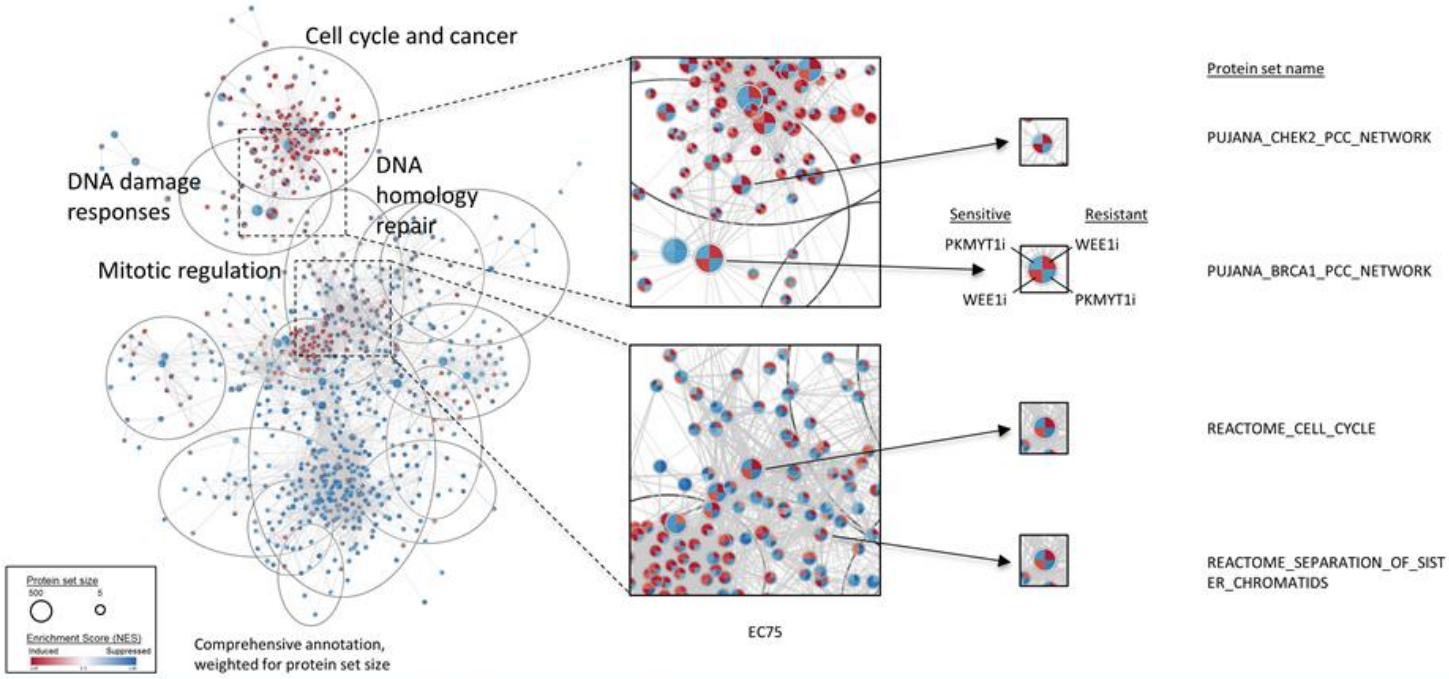


Kinase activity based on proprietary PTM-SEA-based hybrid workflow and analyses

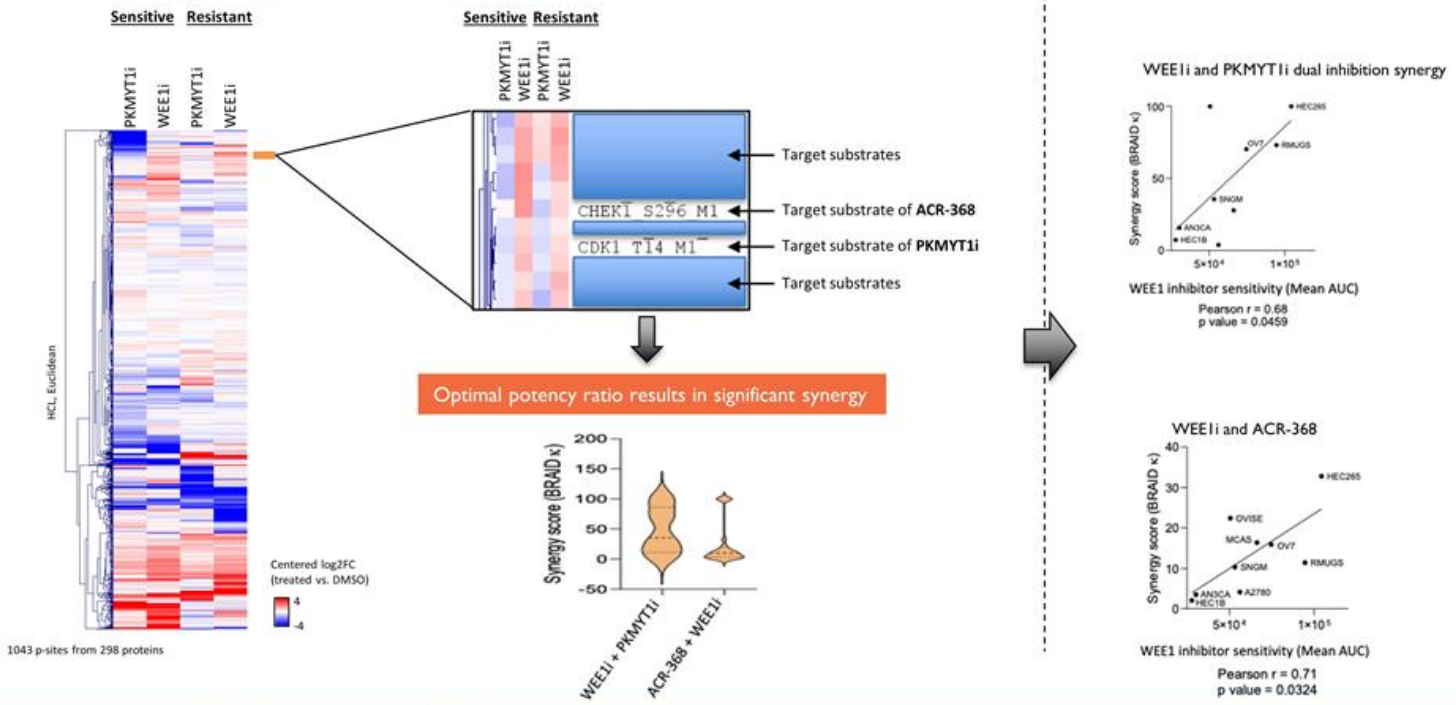


*Clinical-stage selective WEE1 and PKMYT1 inhibitors

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 structure-activity relationship (SAR)
- AP3-enabled design with optimized WEE1 / PKMYT1 properties
- AP3-based optimization of functional target profile

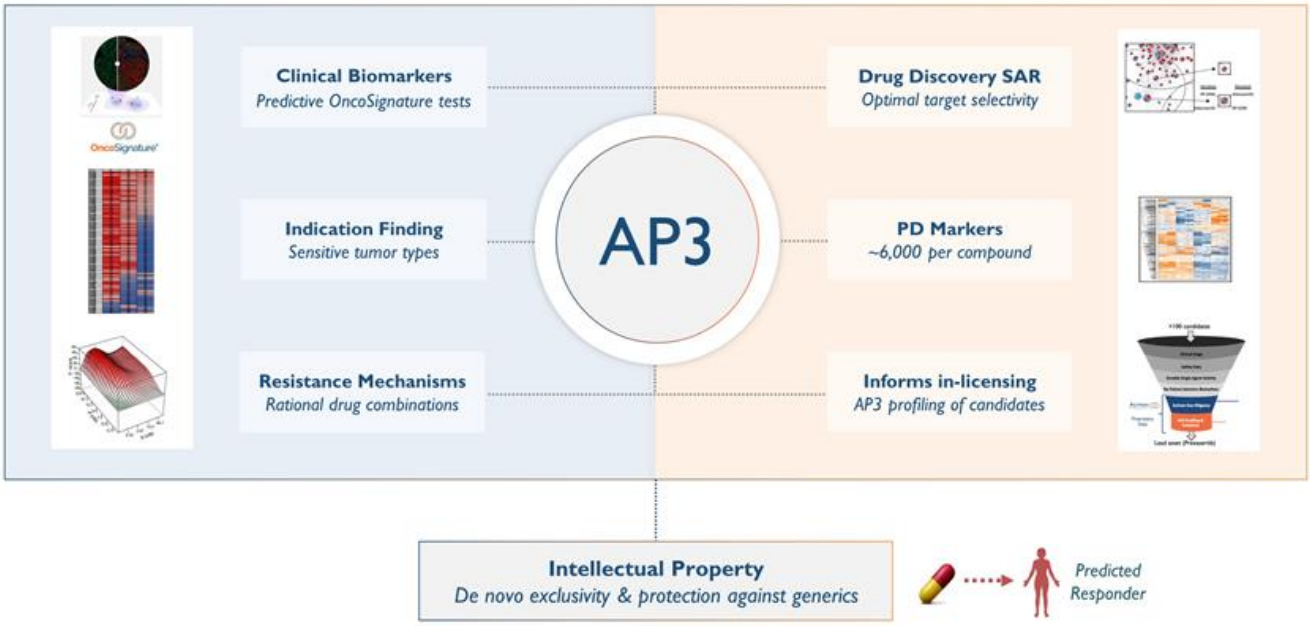
Superior Profile

- Demonstrated preclinical superiority vs. benchmark WEE1 and PKMYT1 compounds
- Stronger preclinical anti-tumor activity vs. benchmark WEE1 and PKMYT1 compounds

Streamlined Development

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

AP3 IS BROADLY APPLICABLE ACROSS DRUG DISCOVERY AND DEVELOPMENT



FINANCIAL HIGHLIGHTS

Cash and marketable securities

$142.1M

Balance sheet 30-Sept-2023

Projected runway into

H2'25

Current operating plan, assuming no additional financing

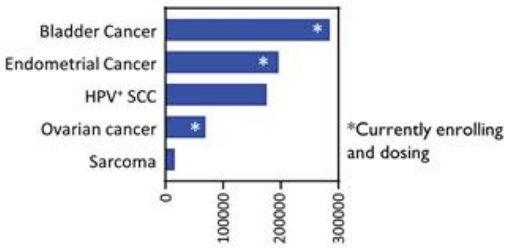
Fully Diluted Shares Outstanding

27.6M

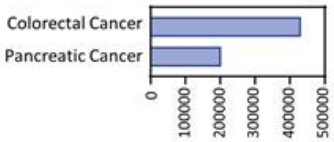
Shares and equity grants outstanding 30-Sept-2023

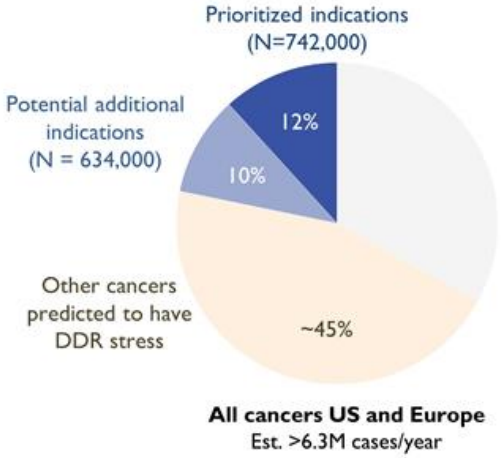
ACRIVON ADDRESSABLE MARKETS (US & EU INCIDENCE)

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

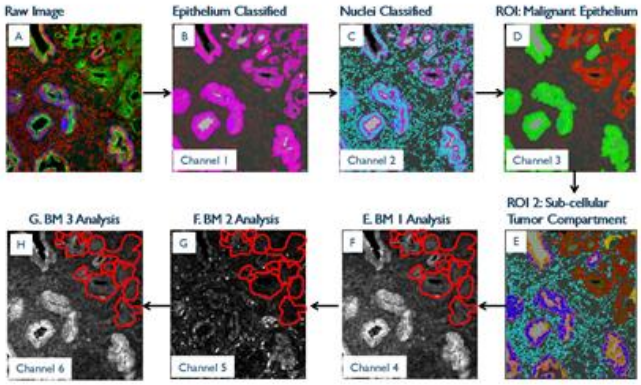
- ~30% (N = 223,000) of prioritized indications predicted sensitive to single agent ACR-368
- WEE1 and/or PKMYT1 inhibitor combinations with ACR-368 might further expand addressable fraction within sensitive tumor types

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)

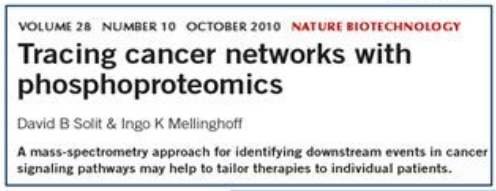
RESEARCH ARTICLE

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,[4,5] Peter Blume-Jensen,[1]‖ Cloud P. Paweletz[1]

Editorial Highlights:

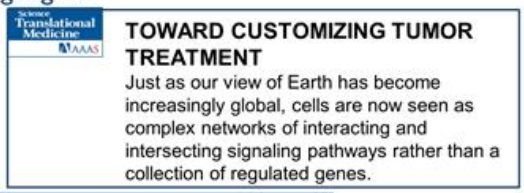


VOLUME 28 NUMBER 10 OCTOBER 2010 NATURE BIOTECHNOLOGY

Tracing cancer networks with phosphoproteomics

David B Solit & Ingo K Mellinghoff

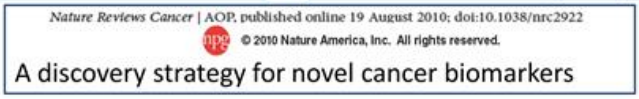
A mass-spectrometry approach for identifying downstream events in cancer signaling pathways may help to tailor therapies to individual patients.



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

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

OPEN

Spatial-proteomics reveals phospho-signaling dynamics at subcellular resolution

Nature Communications (2021)

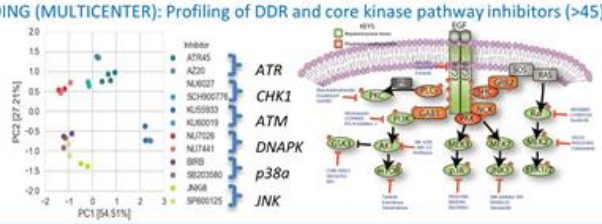
Clinically actionable resistance mechanisms

ARTICLE

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

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Adj. Prof. UCSD

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- Professor, Burnham Institute
- Professor, Duke University

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- Lead/P.I. on numerous DDR trials

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- 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

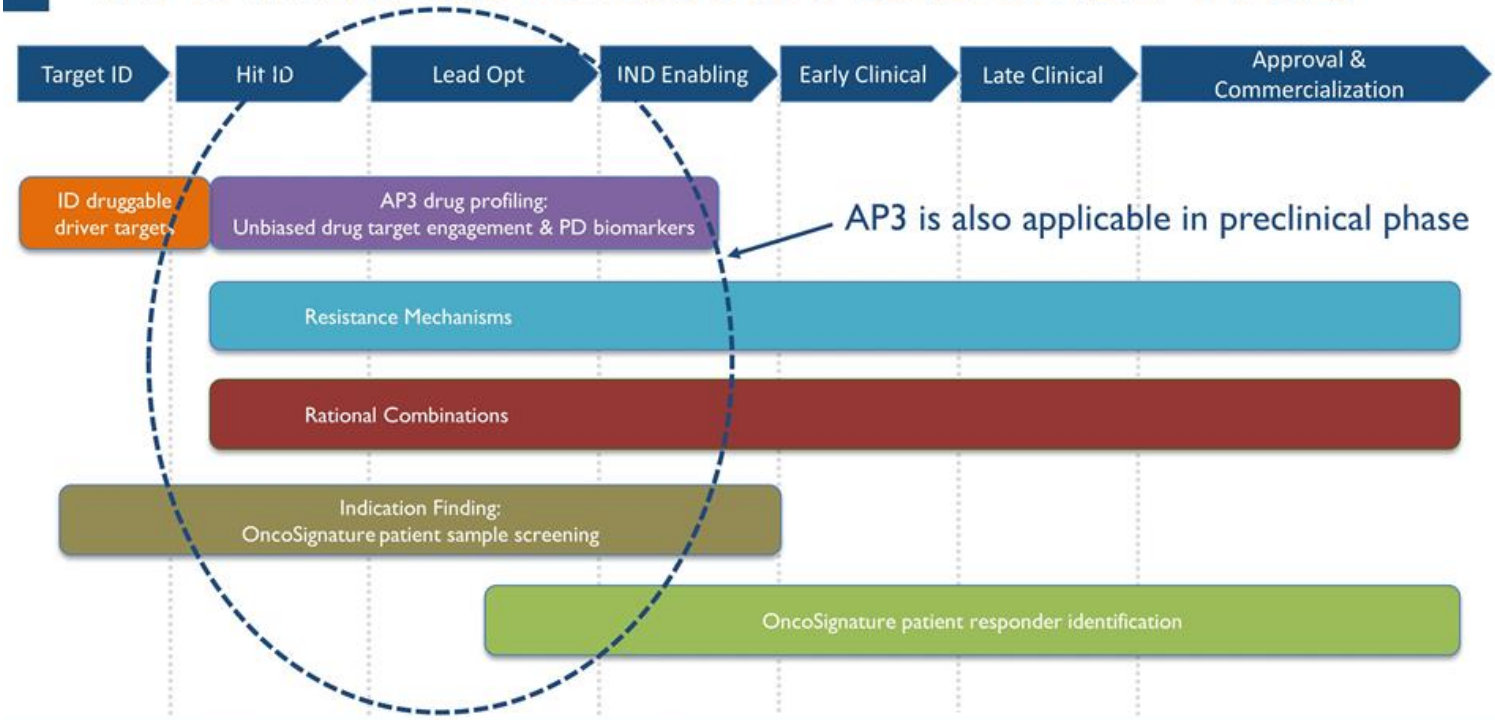
Jung-Min Lee, M.D.

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



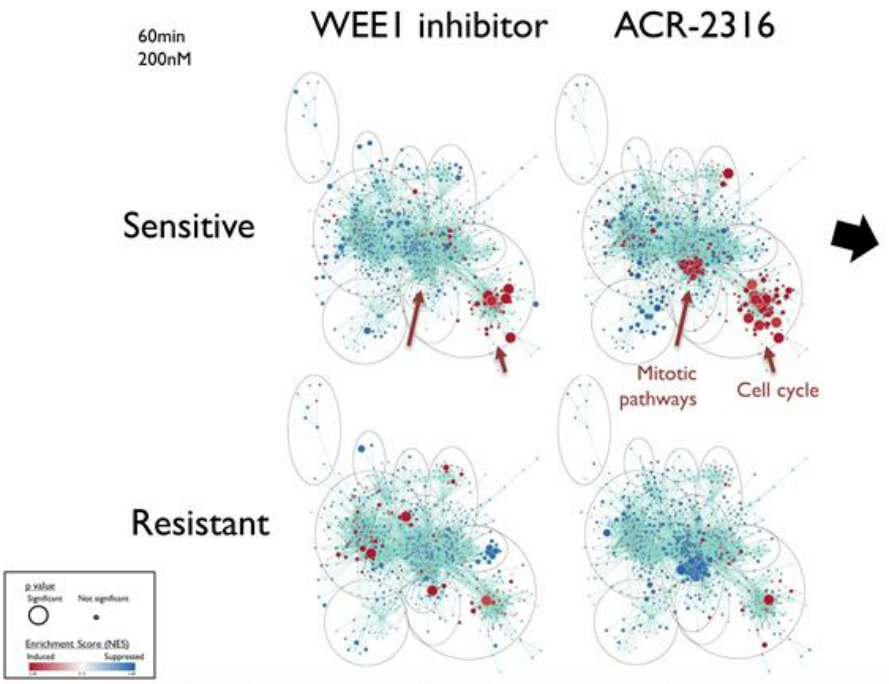
ACR-2316 MEETS PRE-SPECIFIED DEVELOPMENT CANDIDATE CRITERIA

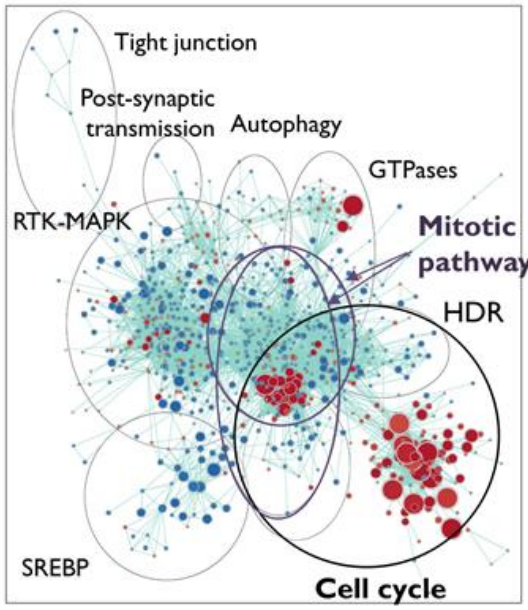
	Target	ACR-2316
MOA	• AP3 phosphoproteomics-based, optimized MOA; selective, dual WEE1/PKMYT1 inhibition	✓
Potency	• In vitro kinase activity, $IC_{50} \leq 10$ nM • Potent *in cell* target engagement in optimized ratio • Activity across sensitive human tumor cell lines, $IC_{50} < 20$ nM	✓ ✓ ✓
Selectivity	• 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

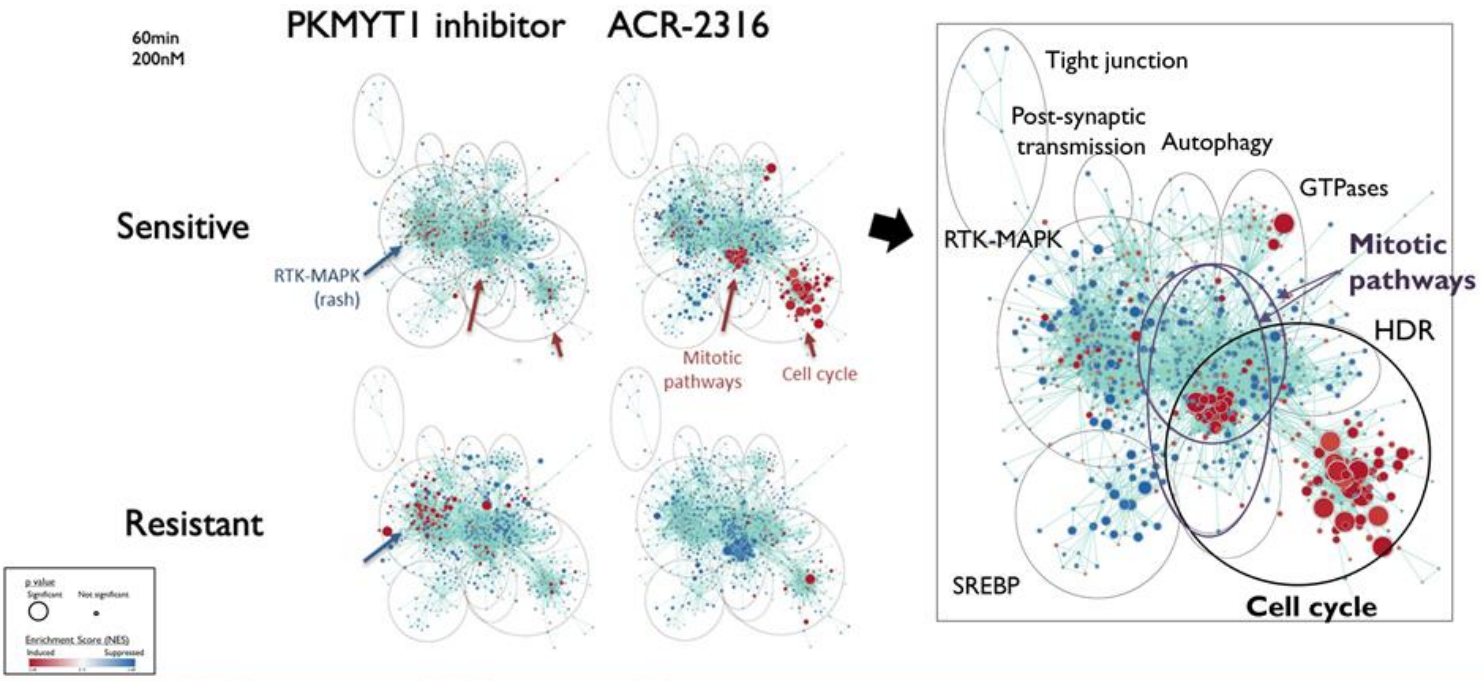
	Assay	ACR-2316	Adavosertib	Azenosertib	Debio123	Lunresertib
Biochemical	Wee1 Binding IC_{50}	1 nM	1 nM	2 nM	1 nM	31 nM
	PKMYT1 Binding IC_{50}	27 nM	155 nM	337 nM	2 µM	10 nM
Cellular Target Engagement	WEE1 EC_{50} (Y15)	2 nM	19 nM	16 nM	109 nM	>10 µM
	PKMYT1 EC_{50} (T14 AlphaLISA)	145 nM	4 µM	2 µM	>10 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

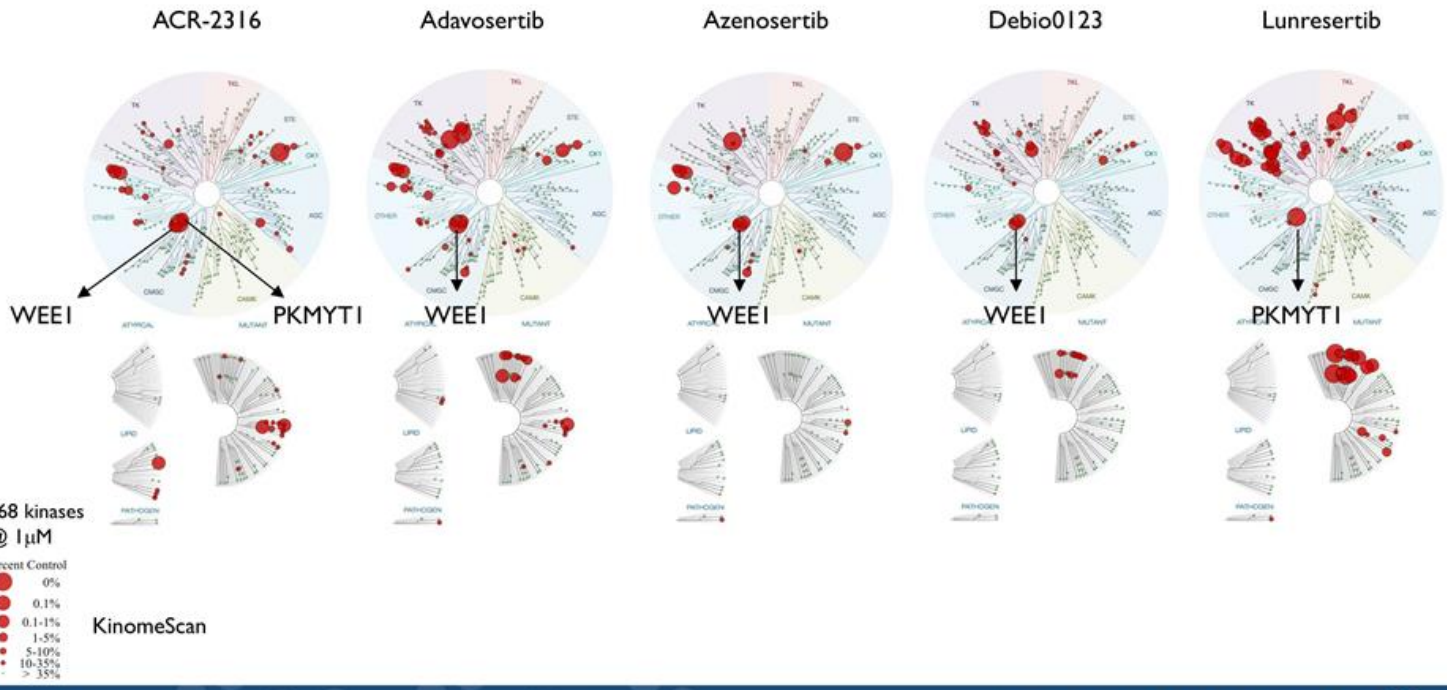




AP3 ANALYSIS: ACR-2316 REGULATES CELL CYCLE AND MITOSIS MORE POTENTLY THAN BENCHMARK PKMYT1 INHIBITOR



COMPREHENSIVE KINOME SELECTIVITY PROFILING



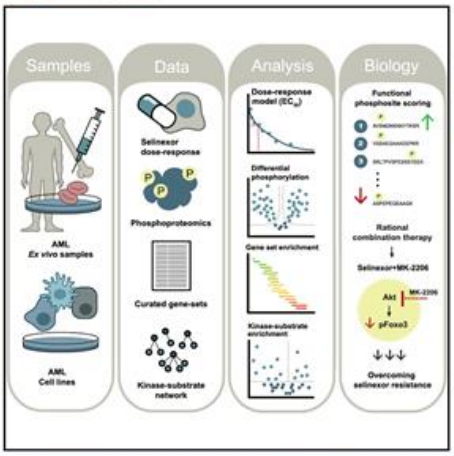
AP3 REVEALS SINGLE AGENT SENSITIVITY CONTEXT AND RATIONAL DRUG COMBINATIONS INDEPENDENT OF GENETIC INFORMATION

Article

Cell Reports

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

Graphical abstract



Authors

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

Correspondence

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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