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): September 5, 2023

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

On September 5, 2023, Acrivon Therapeutics, Inc. (the "Company") issued a press release regarding ACR-2316, its internally developed small molecule development candidate. The Company has also updated its corporate presentation. The presentation provides, among other things, an update regarding the Company's pipeline, including ACR-2316, disclosure regarding the Company's cash and marketable securities as of June 30, 2023 and confirmation of its projected cash runway into 2025.

Copies of the Company's press release and corporate presentation are attached hereto as Exhibit 99.1 and Exhibit 99.2 and are 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	Press release, dated September 5, 2023
99.2	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: September 5, 2023

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

Acrivon Therapeutics Announces ACR-2316, a Novel Dual WEE1 and PKMYT1 Inhibitor Development Candidate, Designed Using Acrivon's AP3 Platform to Achieve Potent Single Agent Activity, as Demonstrated in Preclinical Studies

Acrivon's Predictive Precision Proteomics (AP3) platform is a proprietary, broadly applicable, next-generation precision oncology platform at the forefront of the next wave of biology-driven drug discovery, in addition to its previously demonstrated utility in clinical development for treating patients based on predicted drug sensitivity

ACR-2316 is a novel, internally developed small molecule development candidate, rationally designed through advanced co-crystallography and the AP3 platform to achieve optimal target potency and selectivity delivering potent single agent anti-tumor activity across in vitro and in vivo preclinical studies, compared to benchmark WEE1 and PKMYT1 inhibitors

The AP3 platform has uniquely enabled the rapid generation of this novel dual inhibitor optimized to potentially overcome resistance mechanisms induced by WEE1 and PKMYT1 single inhibitors, and other mechanism-based liabilities

The company is prioritizing advancement of this molecule, with planned IND submission by the fourth quarter of 2024, to initiate clinical monotherapy development in tumor types predicted responsive to ACR-2316 through prior AP3-derived OncoSignature indication finding and subsequent treatment of patients based on OncoSignature-predicted sensitivity

WATERTOWN, Massachusetts, September 5, 2023 – Acrivon Therapeutics, Inc. ("Acrivon" or "Acrivon Therapeutics") (Nasdaq: ACRV), a clinical stage biopharmaceutical company developing precision oncology medicines that it matches to patients whose tumors are predicted to be sensitive to each specific medicine by utilizing its proprietary proteomics-based patient responder identification platform, today announced a novel, internally developed clinical candidate, ACR-2316, a dual WEE1 and PKMYT1 inhibitor. The company plans to prioritize Investigational New Drug (IND) enabling studies for ACR-2316 to be ready for IND submission by the fourth quarter of 2024.

"The rapid generation and optimized design of ACR-2316 further demonstrates the broad utility of the AP3 platform in drug discovery, in addition to its applications in clinical development," said Kristina Masson, Ph.D., M.B.A., co-founder, executive vice president, and site head of Acrivon AB, Acrivon Therapeutics' wholly-owned drug discovery and phosphoproteomics subsidiary in Medicon Village, Lund, Sweden. "This dual inhibitor development candidate is yet another powerful validation of our AI-enabled AP3 platform, which has been instrumental for the identification of this compound, optimized for strong single agent activity compared to existing WEE1 and PKMYT1 inhibitors."

“Previously, we have shown how AP3 can be used to develop drug-tailored predictive OncoSignature tests for effective identification of patients likely to respond to a given therapy, as we have done for our clinical stage CHK1/2 inhibitor, ACR-368,” said Peter Blume-Jensen, M.D., Ph.D., chief executive officer, president, and founder of Acrivon Therapeutics. “We now believe that we have shown how AP3 can be used to go beyond the limitations of traditional drug discovery methods by enabling biological pathway-based rational design of development candidates with optimal target selectivity profile and potency, with ACR-2316 being the first example. This novel dual WEE1/PKMYT1 inhibitor has the potential to address significant unmet needs across many solid tumor types based on its compelling preclinical profile, with the potential for monotherapy development in tumors predicted to be sensitive to ACR-2316 using our OncoSignature patient selection approach.”

Based on the emerging favorable preclinical profile of ACR-2316, the company has entered into IND-enabling studies. The compound is designed for high selectivity towards WEE1 and PKMYT1, exhibiting single-digit nM IC_{50} potency in a carefully predetermined ratio to ensure strong single agent anti-tumor activity, as demonstrated in tumor-bearing rodent models and other preclinical analyses. Using AP3 for unbiased quantitative high-resolution measurement of the effects of ACR-2316 on the human tumor cell phosphoproteome, this compound has been further optimized for potent induction of mitotic catastrophe, which is key to its strong single agent activity in preclinical models and potentially favorable clinical profile for monotherapy development.

“The preclinical data we have generated thus far is consistent with potential clinical advantages and possible differentiation compared to current single inhibitors of WEE1 and PKMYT1, both critically important cell cycle regulators with demonstrated clinical activity,” said Erick Gamelin, M.D., Ph.D., chief medical officer of Acrivon. “We are particularly encouraged by its compelling target selectivity and preclinical potency profile. With ACR-2316, we have demonstrated that the company’s data-driven, streamlined AP3 approach can generate molecules with desirable preclinical properties tailored for clinical monotherapy development.”

Additional information regarding ACR-2316 can be found in the company’s updated corporate presentation, which can be found on the company’s website using this link.

About Acrivon Therapeutics

Acrivon is a clinical stage biopharmaceutical company developing precision oncology medicines that it matches to patients whose tumors are predicted to be sensitive to each specific medicine by utilizing Acrivon’s proprietary proteomics-based patient responder identification platform, Acrivon Predictive Precision Proteomics, or AP3. The AP3 platform enables the creation of drug-specific proprietary OncoSignature companion diagnostics that are used to identify the patients most likely to benefit from Acrivon’s drug candidates. Acrivon is currently advancing its lead candidate, ACR-368, a selective small molecule inhibitor targeting CHK1 and CHK2 in a potentially registrational Phase 2 trial across multiple tumor types. The company has received fast track designation from the Food and Drug Administration, or FDA, for the investigation of ACR-368 as monotherapy based on OncoSignature-predicted sensitivity in patients with platinum-resistant ovarian or endometrial cancer. Acrivon’s ACR-368 OncoSignature test, which has not yet obtained regulatory approval, has been extensively evaluated in preclinical studies, including in two separate, blinded, prospectively-designed studies on pretreatment tumor biopsies collected from past third-party Phase 2 trials in patients with ovarian cancer treated

with ACR-368. In addition to ACR-368, Acrivon is also leveraging its proprietary AP3 precision medicine platform for developing its internally-discovered preclinical stage pipeline programs, consisting of its development candidate, ACR-2316, a selective, dual WEE1/PKMYT1 inhibitor, and additional programs targeting these two critical nodes in the DNA Damage Response, or DDR, pathways.

Forward-Looking Statements

This press release includes certain disclosures that contain “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this press release, including statements regarding our future results of operations or financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. 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,” “possible,” “predict,” “project,” “should,” “target,” “will,” or “would” or the negative of these words or other similar terms or expressions. Forward-looking statements are based on Acrivon’s current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, risks and uncertainties that are described more fully in the section titled “Risk Factors” in our reports filed with the Securities and Exchange Commission. Forward-looking statements contained in this press release are made as of this date, and Acrivon undertakes no duty to update such information except as required under applicable law.

Investor and Media Contacts:

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alevy@acrivon.com

Alexandra Santos
asantos@wheelhouselsa.com

Exhibit 99.2

Acrivon Therapeutics

ACRIVON PREDICTIVE PRECISION PROTEOMICS (AP3): DRUG-TAILORED PATIENT SELECTION FOR CLINICAL SUCCESS

CORPORATE PRESENTATION

SEPTEMBER 2023

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.

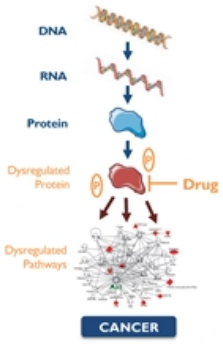
You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this presentation. We undertake no obligation to update any forward-looking statements or to reflect new information or the occurrence of unanticipated events, except as required by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

ACRIVON THERAPEUTICS: DRUG-TAILORED PATIENT SELECTION

AIMING TO OVERCOME THE KEY ATTRITION FACTOR PREVENTING CLINICALLY ACTIVE DRUGS FROM REACHING MARKET

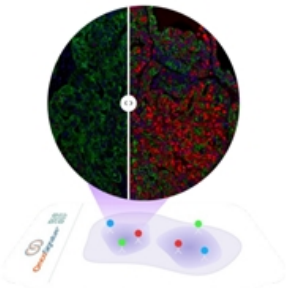
AP3 Platform

- Acrivon's proprietary proteomics-based predictive precision medicine platform
- Applied where NGS/genetics is insufficient and for our internal pipeline



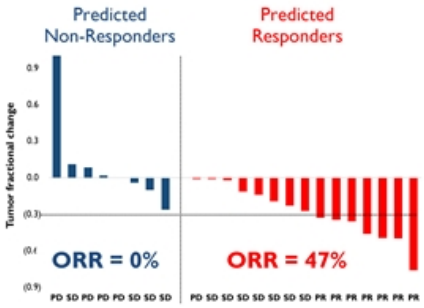
OncoSignature Test

- Our proprietary predictive drug-tailored biopsy test
- Extensively evaluated in prospective preclinical studies, including on blinded pretreatment tumor biopsies from past trials



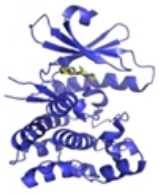
ACR-368 (Prexasertib)

- Clinically active (15-20% ORR) Phase 2 DNA Damage Response (DDR) inhibitor licensed from Eli Lilly & Co.
- Now being developed with OncoSignature patient selection for increased ORR with registrational intent



Pipeline

- Monotherapy candidate ACR-2316, a selective, dual WEE1/PKMYT1 inhibitor, in IND-enabling studies
- Additional co-crystallography programs leveraging AP3 to optimize target selectivity profile and indication finding for monotherapy



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 AP3 pt. selection platform

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

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

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

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

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)

Mary-Alice Miller, J.D.
SVP, General Counsel

Adam Levy, Ph.D., M.B.A.
SVP, Investor Relations and Corporate Affairs

Praveen Marapaka, Ph.D.
SVP, Global Regulatory Affairs

John van Duzer, Ph.D.
SVP, CMC

Bruce Close
VP, Quality and Compliance

Joon Jung, Ph.D.
VP, Head, Data Science

Parvin Miah
VP, Head, Human Resources

Katie Peterson, C.P.A.
VP, Finance and Accounting

Monica Phadnis
VP, Clinical Operations

David Proia, Ph.D.
VP, Drug Discovery and Biology

Michail Shipitsin, Ph.D.
VP, Biomarker Development

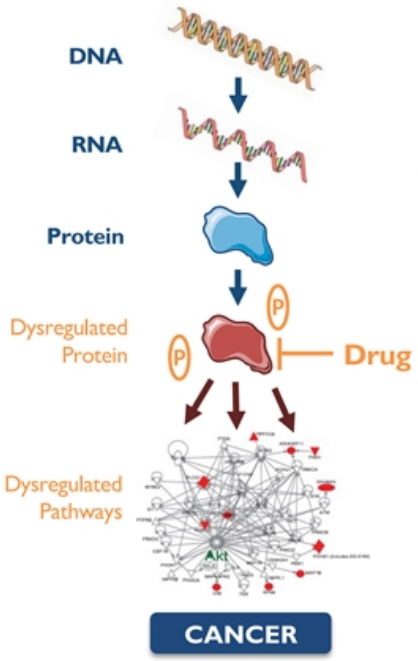
MERCK · MERCK SERONO · Daiichi-Sankyo · AMGEN · MIRATI THERAPEUTICS · Pfizer · Biogen · Roche · Shire · Metamark · MD Anderson Cancer Center · SALK INSTITUTE Where cures begin. · BROAD INSTITUTE · The Novo Nordisk Foundation Center for Protein Research

ACRIVON THERAPEUTICS AT A GLANCE

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*

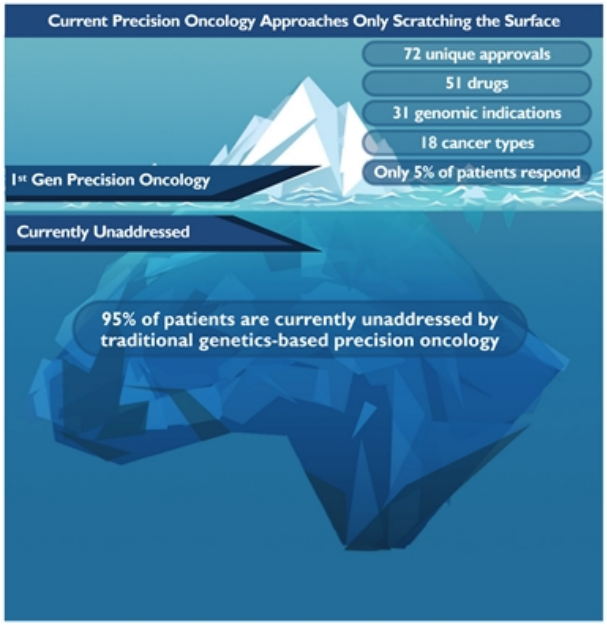
CANCER IS CAUSED BY DYSREGULATED PROTEIN ACTIVITY

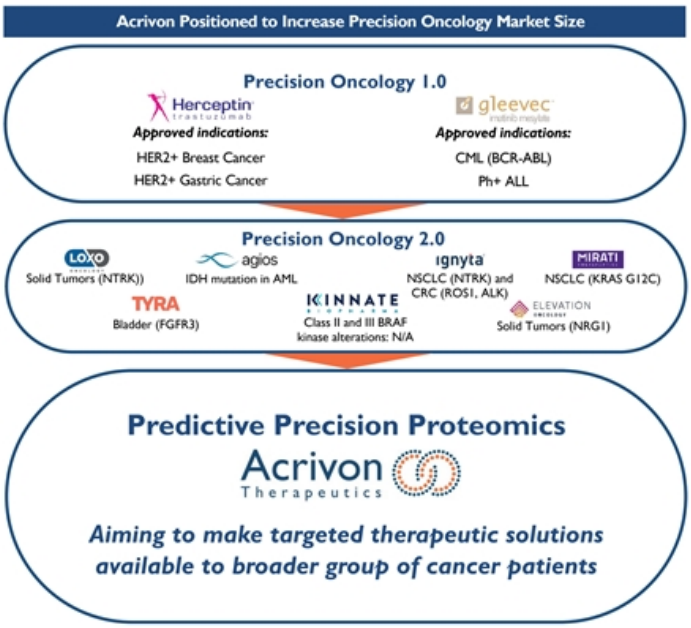
Acrivon's AP3 platform directly measure the disease-driving, dysregulated proteins and is designed to enable an exact match with the drug mechanism-of-action independent of genetic alterations

(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)

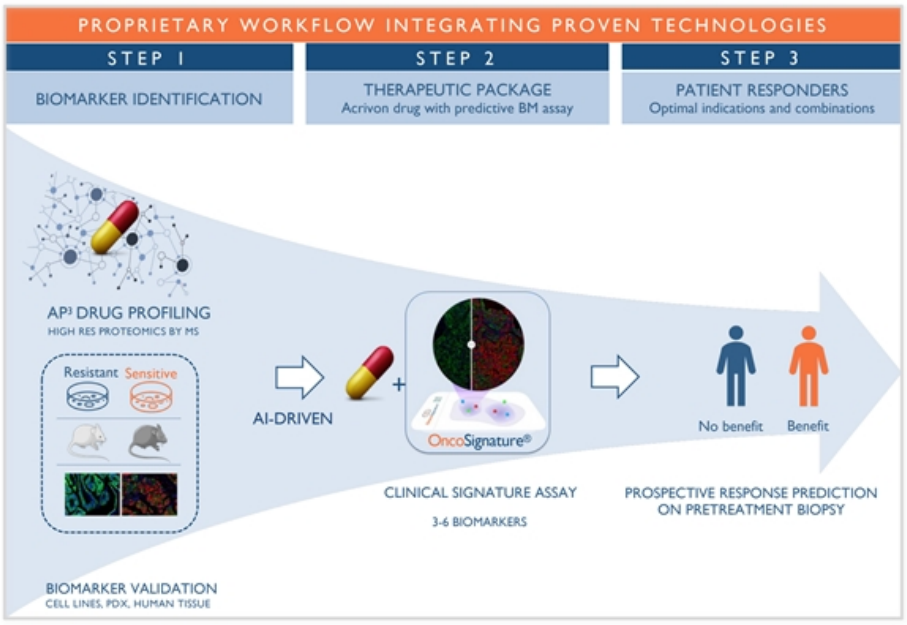
AP3 PLATFORM ADDRESSES HIGH UNMET NEED BEYOND NGS-BASED PRECISION MEDICINE

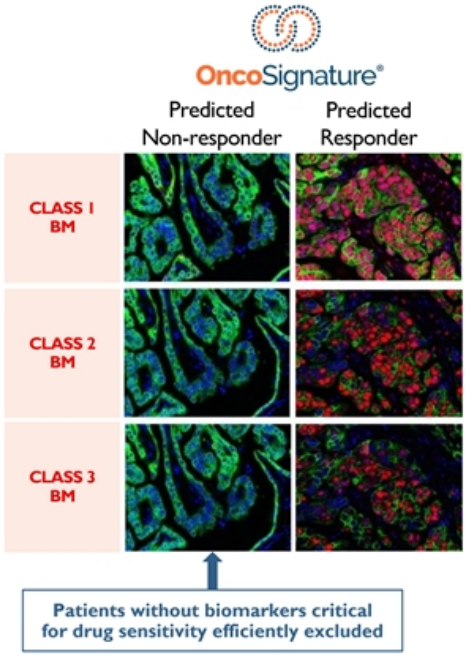




Sources: Company Filings, ACS, CDC, NCI, Wall Street Research

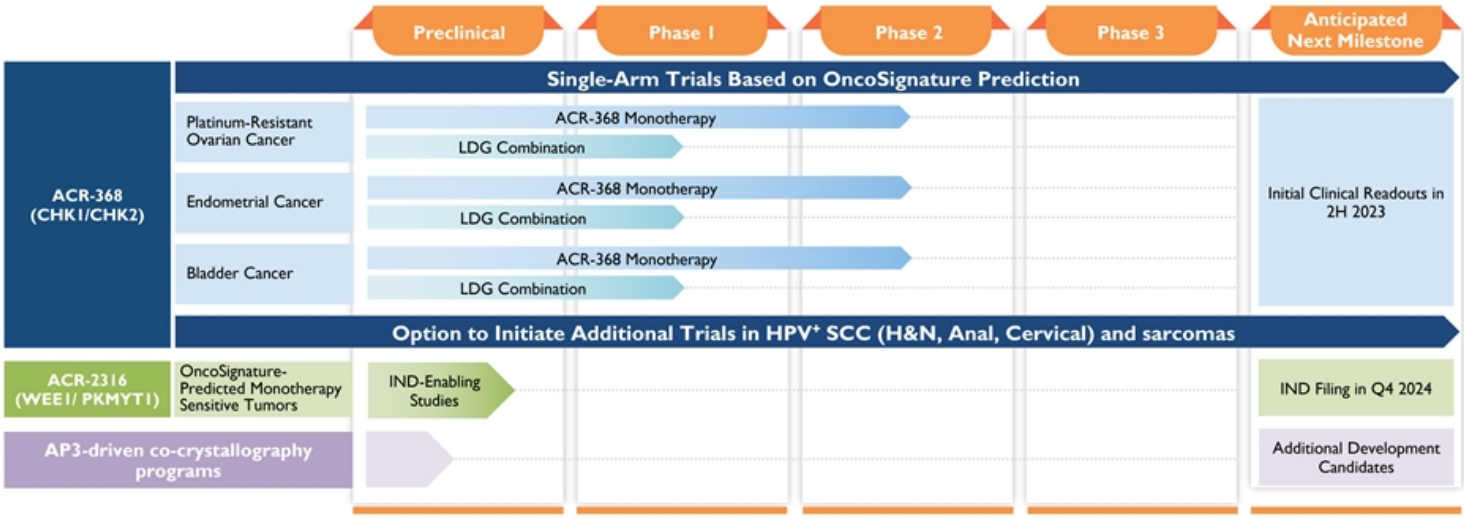
AP3 PLATFORM: DRUG RESPONSE PREDICTION IN INDIVIDUAL PATIENTS





"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

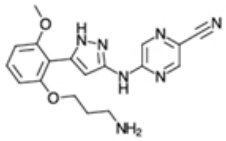


Notes

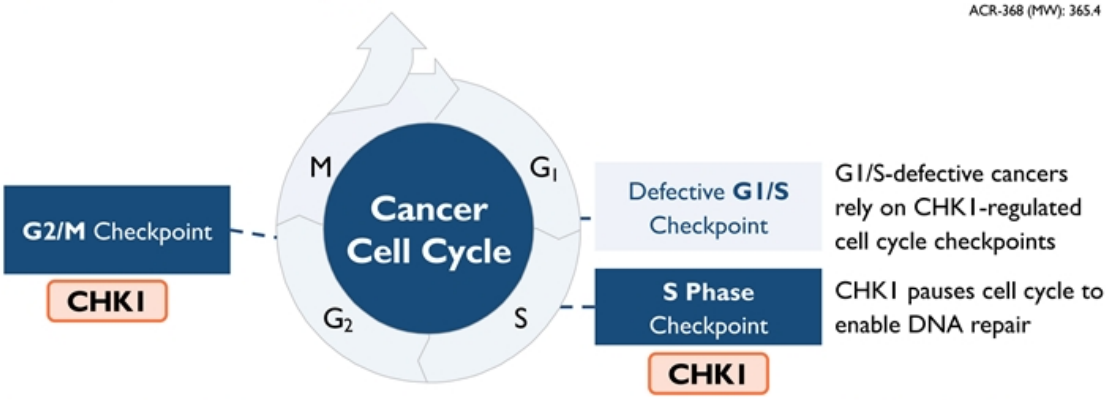
ACR-368 Monotherapy	Registrational intent Phase 2 single arm trials based on predicted sensitivity to ACR-368 monotherapy in OncoSignature-positive patients
LDG Combination	Exploratory Phase 1b/2 single arm trials of ACR-368 in combination with low dose gemcitabine, or LDG, in OncoSignature-negative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

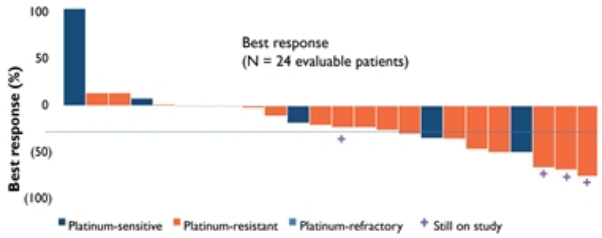
PAST PHASE 2 TRIALS IN HIGH GRADE SEROUS OVARIAN CANCER

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

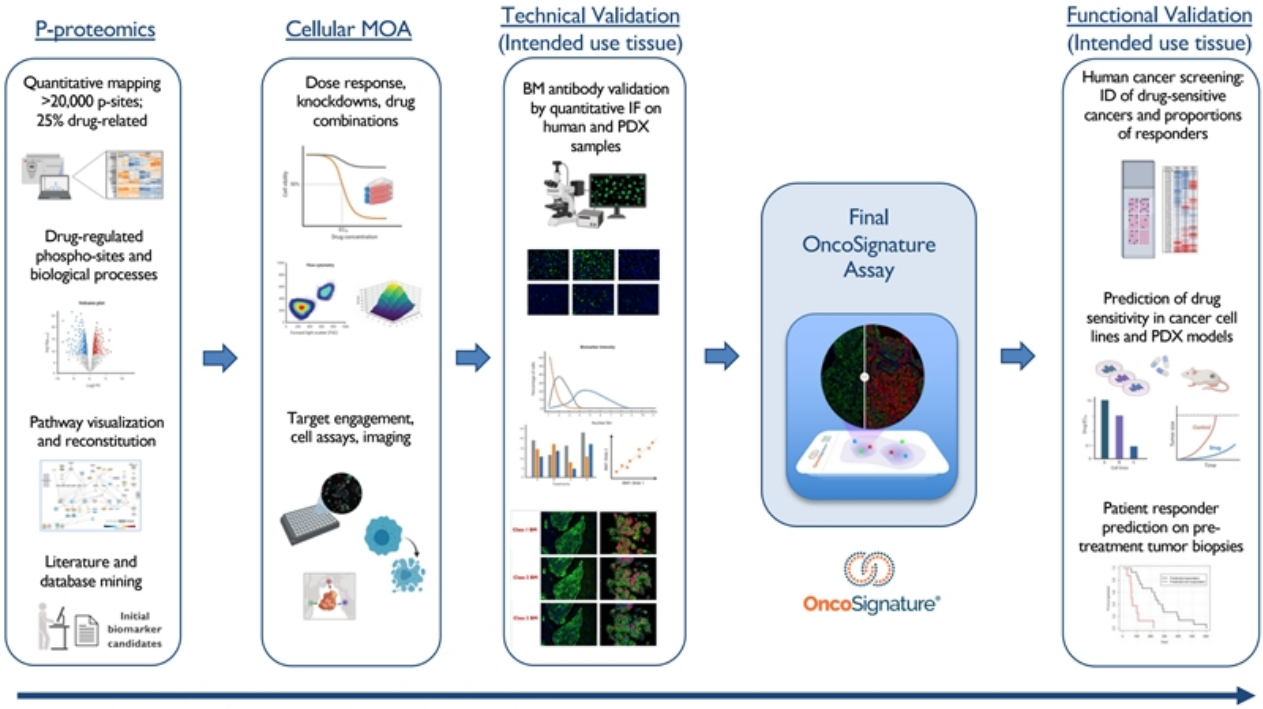
- ORR 12.1% (excl. unconfirmed); mDoR =5.6 months
- No correlation with genetic alterations

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

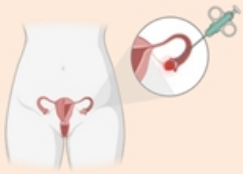
- ✓ Past trials suggest unenriched all-comer ORR in HGS ovarian cancer is ~15-20%
- ✓ Durable clinical activity in most responders
- ✓ No predictive biomarkers identified, need for alternative biomarker approach (ideal for AP3)

DEVELOPMENT OF AP3-BASED PATIENT SELECTION ONCOSIGNATURE TESTS

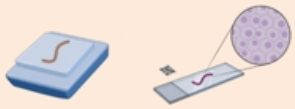


ONCOSIGNATURE TESTS: USAGE IN THE CLINIC

Pretreatment tumor biopsy

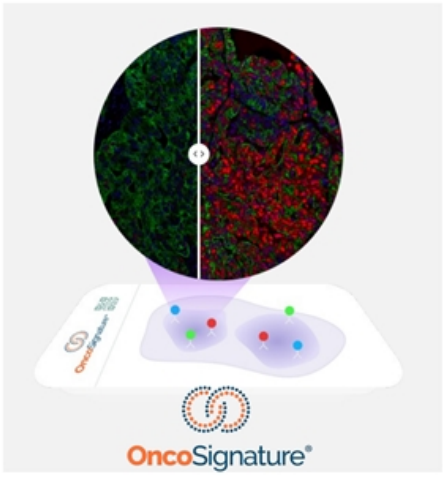


Sample processing



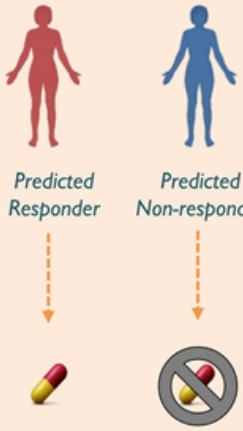
Biopsy in FFPE block

Automated tumor Region-of-Interest biomarker scoring

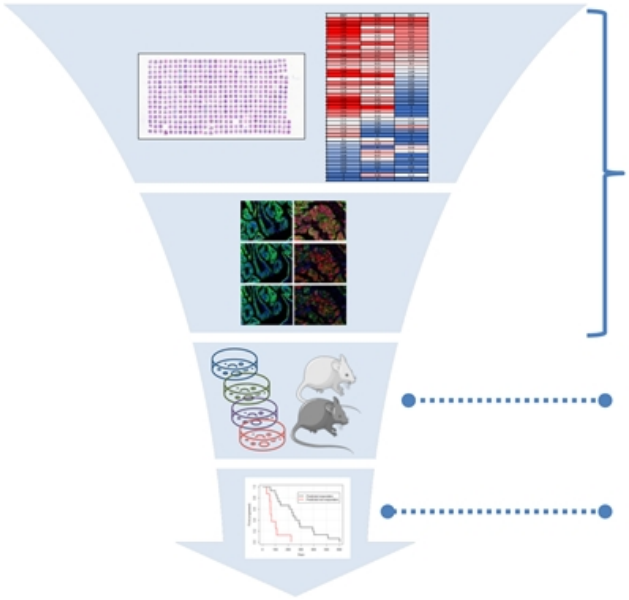


- Pretreatment tumor biopsy test
- Compatible with 5 business days turn-around
- Offered by CDx partner under exclusive license from Acrivon

Treatment decision based on patient stratification



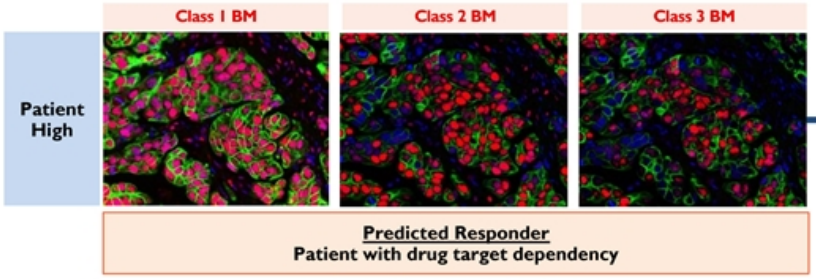
CONSISTENT ACR-368 ONCOSIGNATURE PERFORMANCE ACROSS PRECLINICAL STUDIES



OncoSignature®

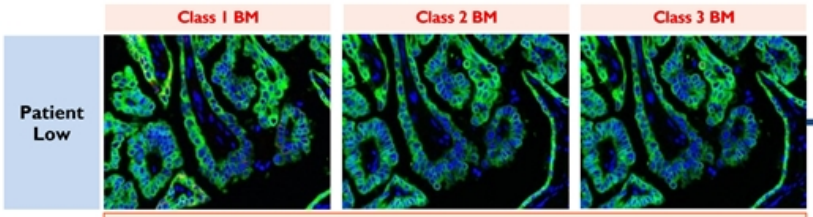
- Prediction of the fraction of human tumors sensitive to single agent ACR-368
  - Selection rate 30-40% across lead indications
- Identification of additional human tumor types predicted sensitive to single agent ACR-368
  - Endometrial and bladder cancer
- Prediction of treatment outcome in human PDX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

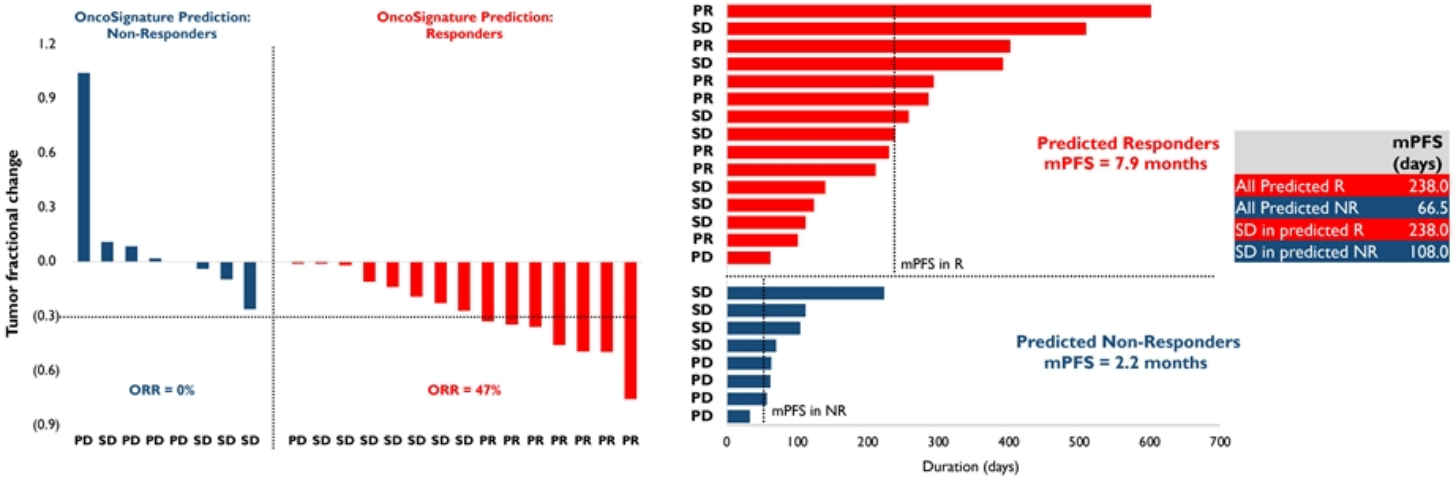


Predicted Non-Responder
Patient with no drug target dependency efficiently excluded

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



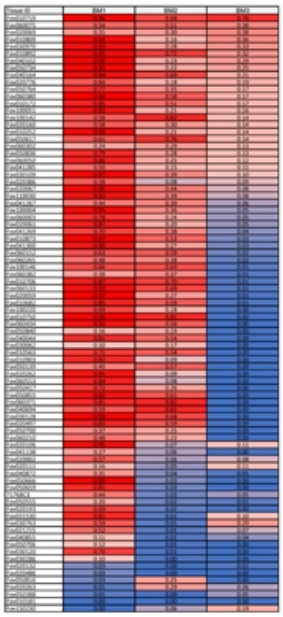
	mPFS (days)
All Predicted R	238.0
All Predicted NR	66.5
SD in predicted R	238.0
SD in predicted NR	108.0

OncoSignature®

Result: ORR ~47%; mPFS = 7.9 months

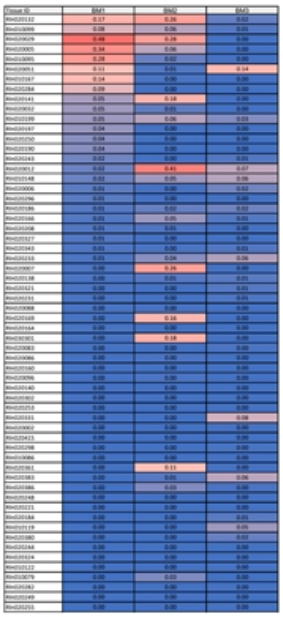
TWO ADDITIONAL HIGH UNMET NEED SOLID CANCERS PREDICTED ACR-368-SENSITIVE THROUGH HUMAN TUMOR SAMPLE SCREENING

HGS Ovarian



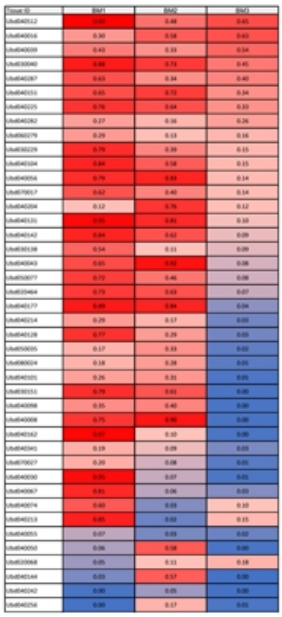
OncoSignature-positive = 30%
(ORR in past trials: 12+% and 29%)

Sq. NSCLC



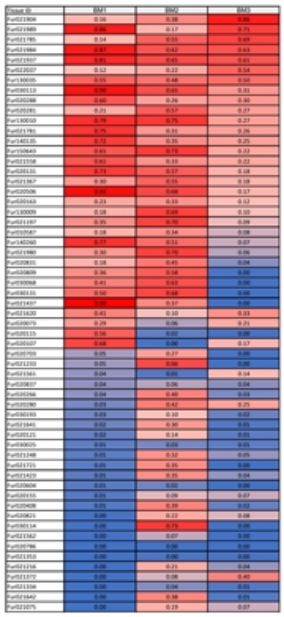
OncoSignature-positive = 0%
(ORR in past trial: 0%)

Bladder cancer



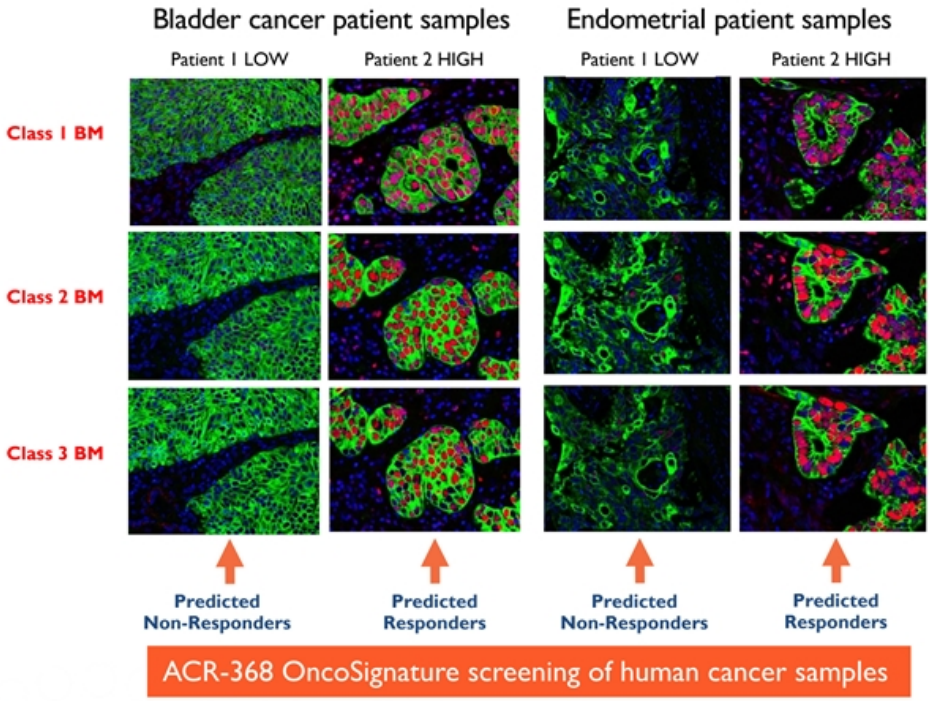
OncoSignature-positive = 30-50%

Endometrial cancer



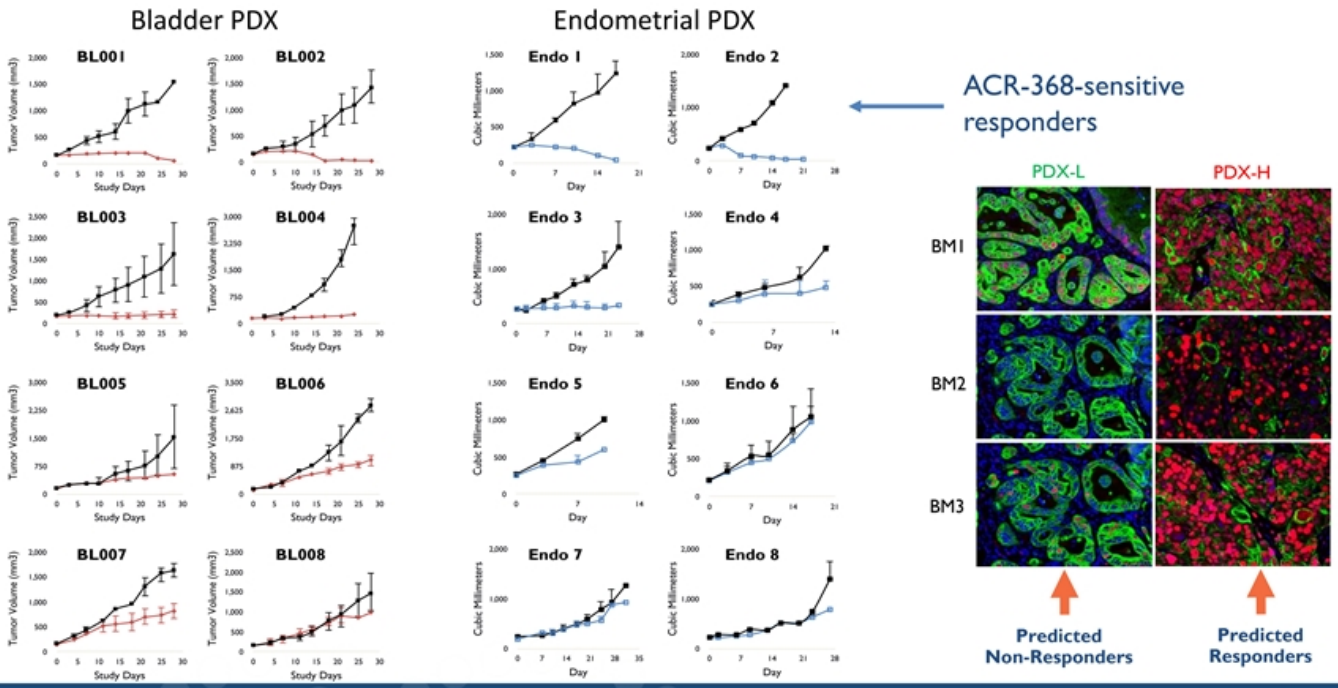
OncoSignature-positive = 30-40%

TWO ATTRACTIVE ACR-368-SENSITIVE CANCER TYPES IDENTIFIED

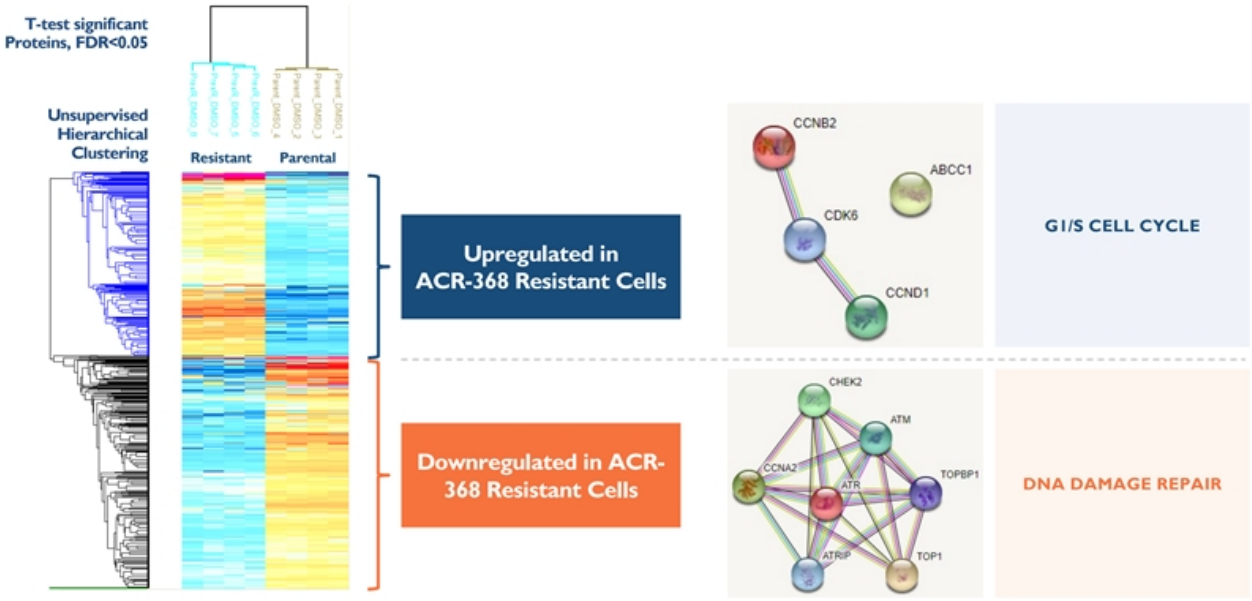


ACR-368 OncoSignature screening of human cancer samples

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

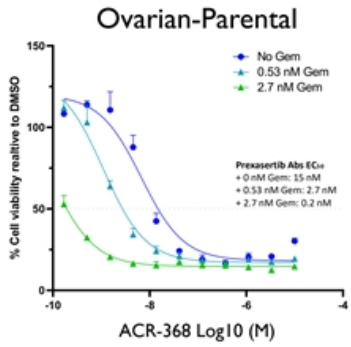


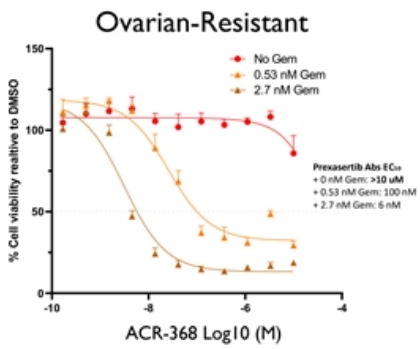
AP3 UNCOVERS ACTIONABLE ACR-368 RESISTANCE MECHANISMS UNBIASED AND INDEPENDENT OF GENETIC INFORMATION

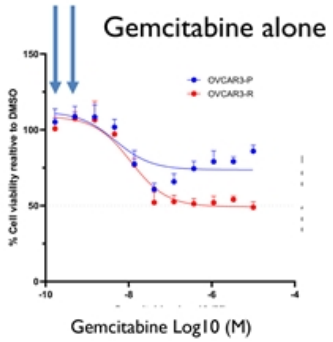


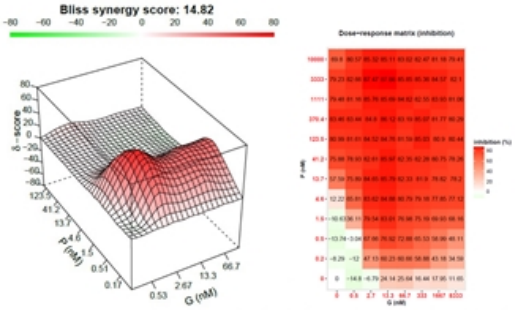
Data suggest that gemcitabine might be a rational combination to overcome DDR suppression

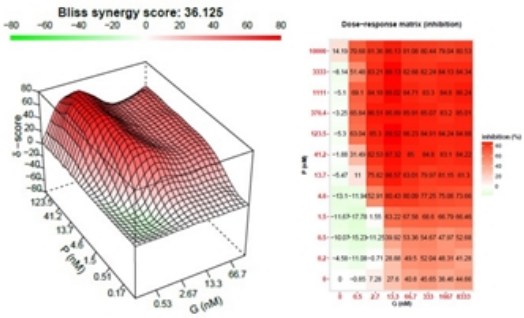
ULTRA-LOW DOSE GEMCITABINE SENSITIZES OVARIAN CANCER CELL LINES TO ACR-368









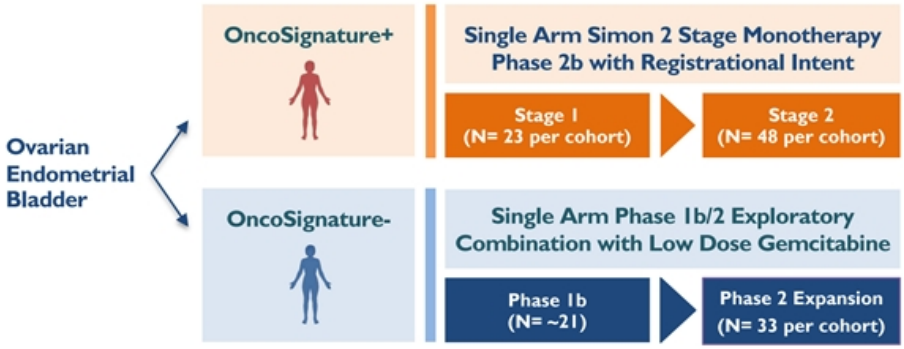


Bliss Synergy score:

- <-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
- 45 sites currently activated[1]
- Key opinion leaders, some with extensive experience using ACR-368 from previous trials are actively participating

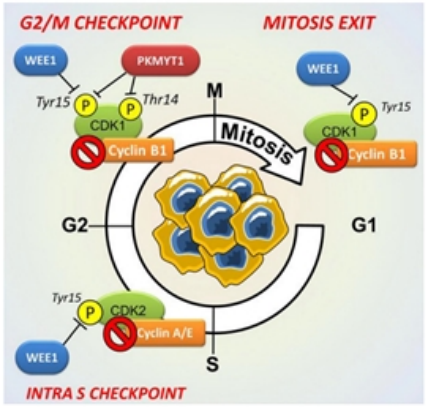


FDA Fast Track Designation granted May 8, 2023 for ACR-368 monotherapy in OncoSignature-positive patients with Platinum-Resistant Ovarian Cancer and Endometrial Cancer

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

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

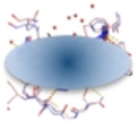
Rationale

- *Leveraging our AP3 patient selection platform for high clinical POS*
- *Potentially optimal profile for monotherapy clinical development and for AP3-identified rational drug combinations*

ACR-2316 and other DDR programs

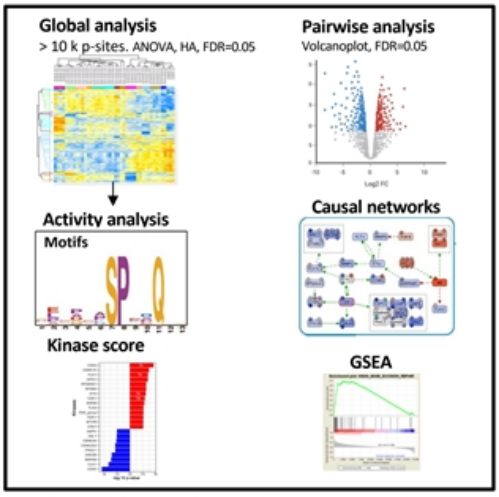
- >39 high resolution co-crystals (1.5-3.1 Å) and AP3-driven SAR
- Novel WEE1- and PKMYT1-selective structural series and lead candidates
- Optimal selectivity profiles generated based on AP3 profiling

ACR-2316 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 single agent activity

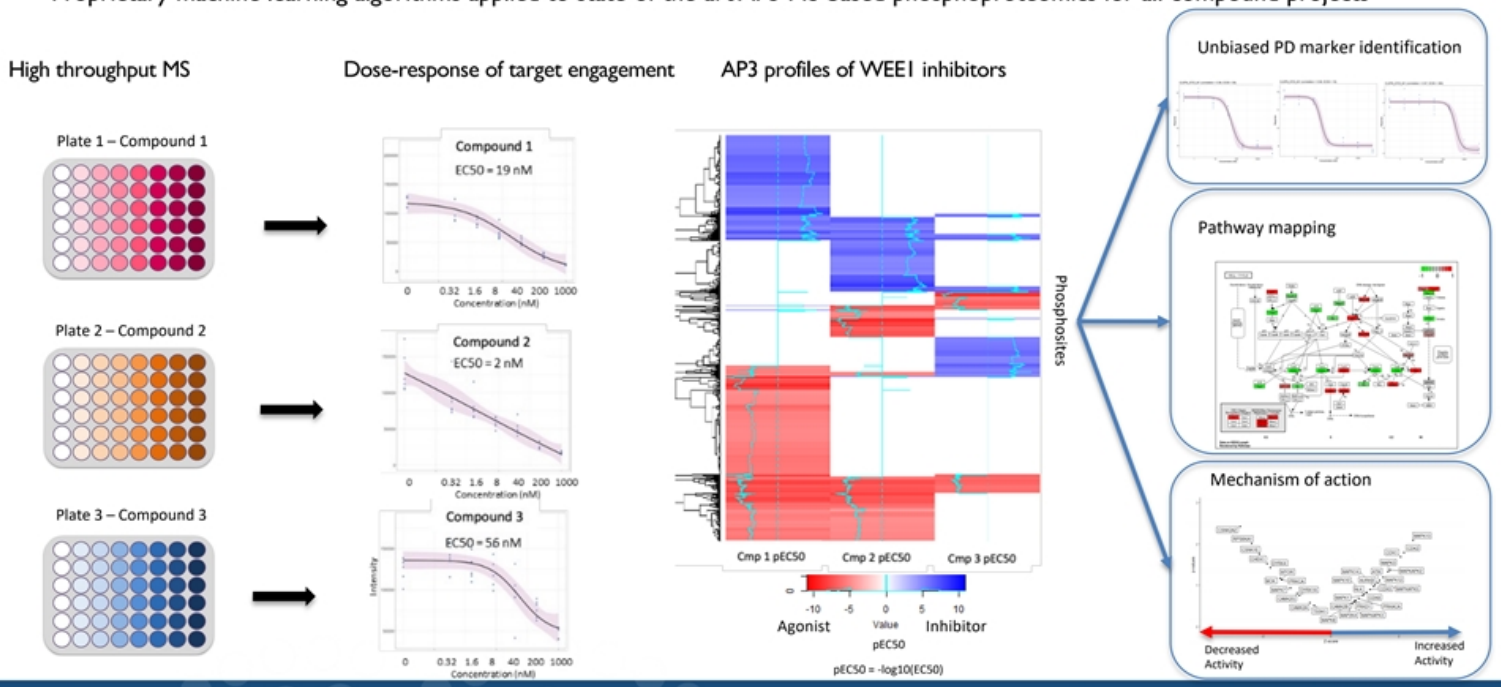
High throughput AP3 profiling



AP3 used for biologically relevant selectivity profiling

AP3 PLATFORM: PROPRIETARY PIPE FOR AUTOMATED ANALYSES WITH ACTIONABLE RESULTS IN ONE DAY

Proprietary machine learning algorithms applied to state-of-the-art AP3 MS-based phosphoproteomics for all compound projects



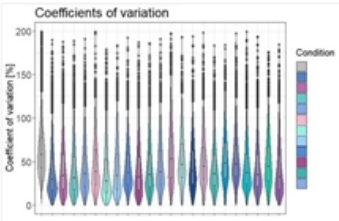
AP3: TIGHT, HIGH-RESOLUTION DATA WITH DEEP COVERAGE

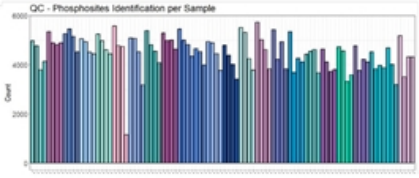
25,800 p-sites

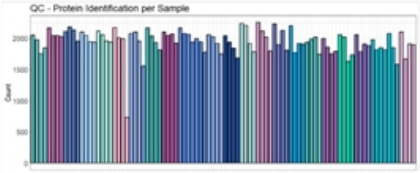
16,456 p-sites

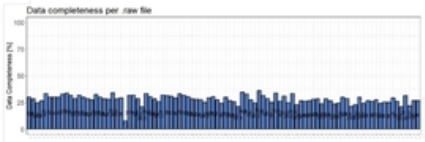
QC MS Data → Data Clean Up → QC Processed Data → Volcano Plots → Hierarchical Clustering → Consensus Sequence Motif → Kinase Inference → Pathway Enrichment → Functional Annotation → Network Mapping → Biomarkers

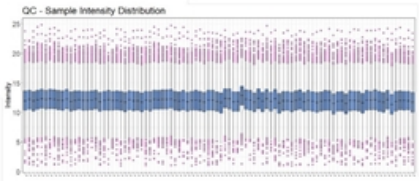
- Filter >60% in at least on condition; Normalization: LOESS; Imputation: SLSA

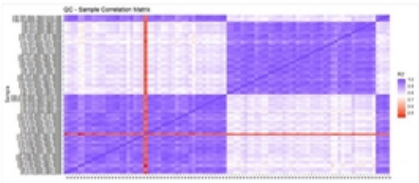








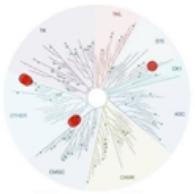




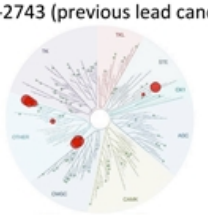
- ✓ Acrivon proprietary compound data (~20 million data points per experiment); dozens of compounds profiled
- ✓ Miniaturized, high throughput, scalable: One week turn-around, automated AI computational analyses in 1 day
- ✓ Actionable results: Resistance mechanisms, rational combinations, drug-tailored OncoSignature patient selection

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

ACR-2316

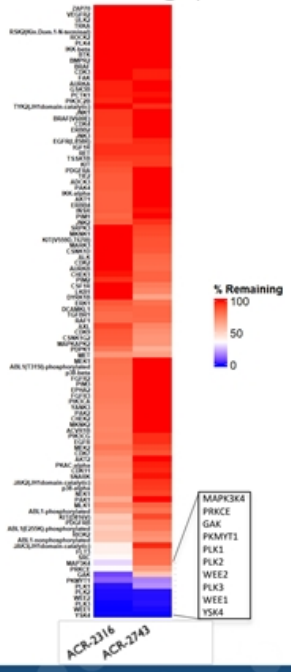


ACR-2743 (previous lead candidate)

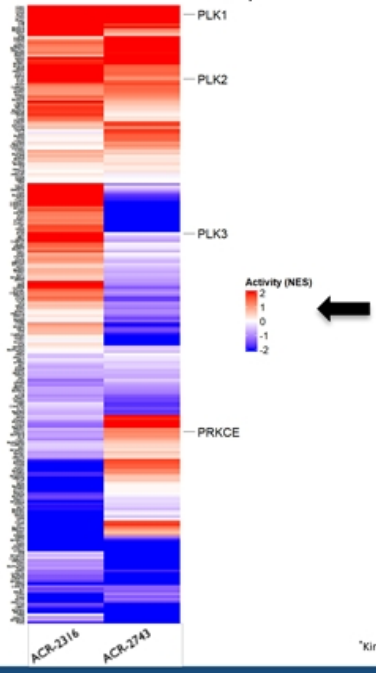


Time : 60 minutes
Dose : 20 nM

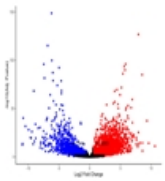
KinomeScan @ 1μM



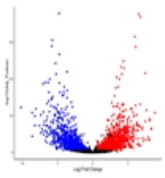
Substrate motif-inferred kinase activity*



ACR-2316

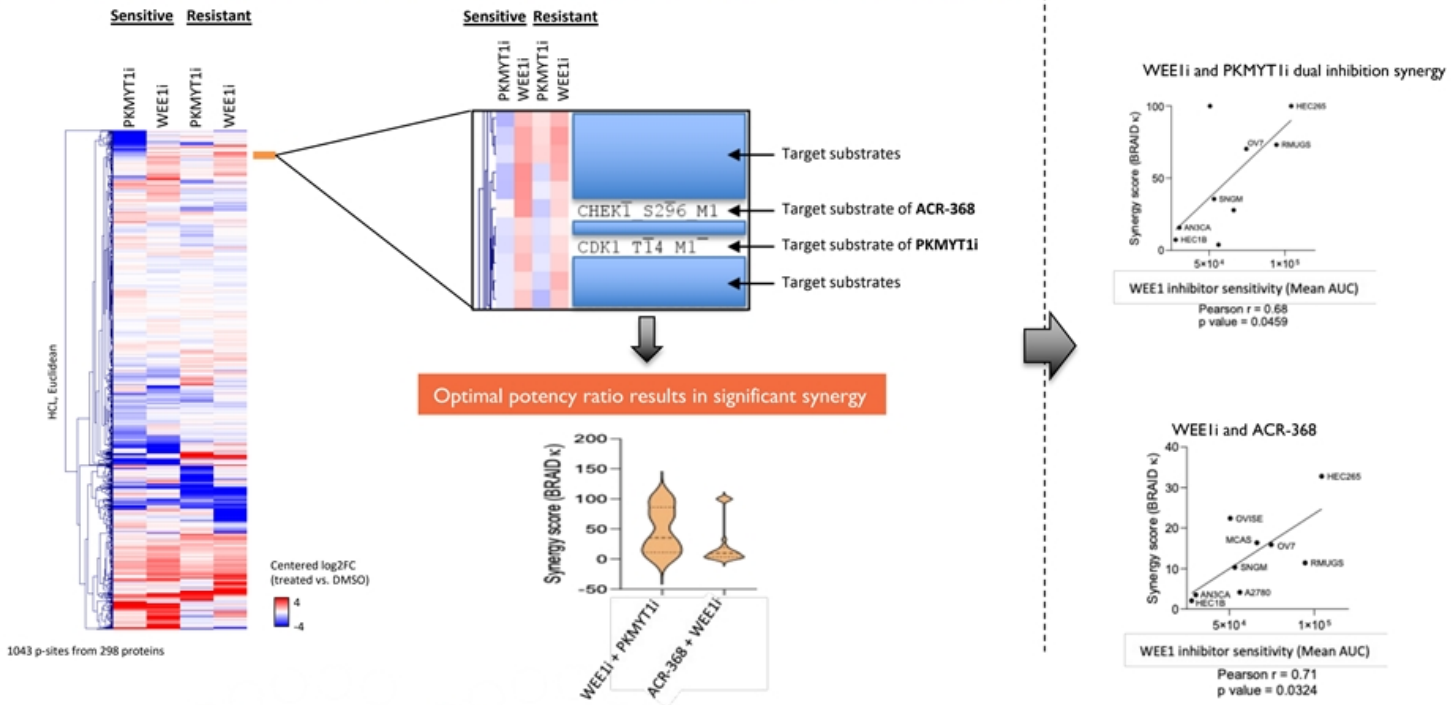


ACR-2743

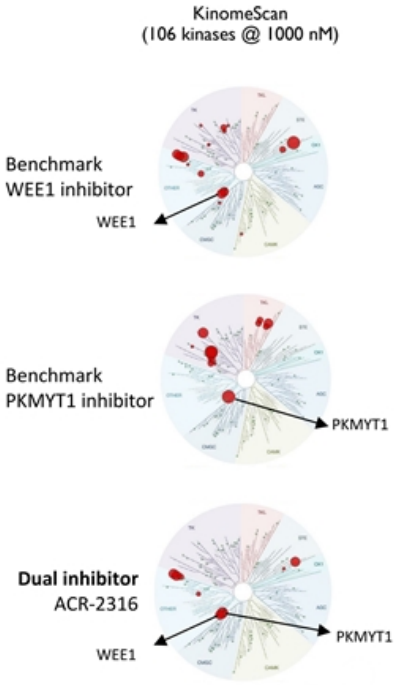


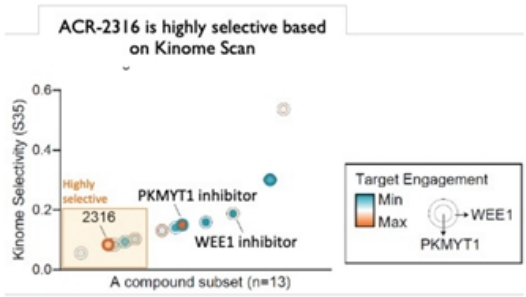
*Kinase activity based on proprietary PTM-SEA hybrid method

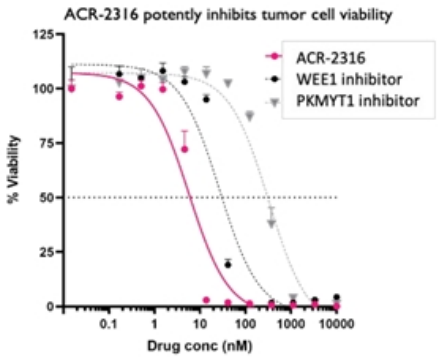
AP3 RECIPROCAL QUENCHING REVEALS OPTIMAL TARGET POTENCY PROFILE FOR DUAL WEE1/PKMYT1 INHIBITOR

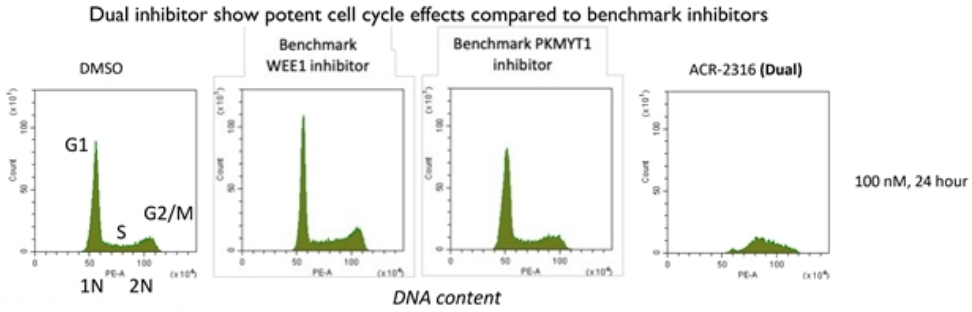


DUAL WEE1/PKMYT1 INHIBITOR ACR-2316 DEMONSTRATES STRONG POTENCY AND SELECTIVITY



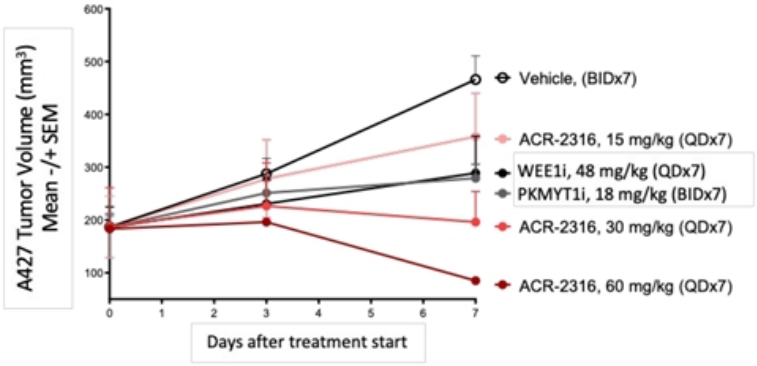




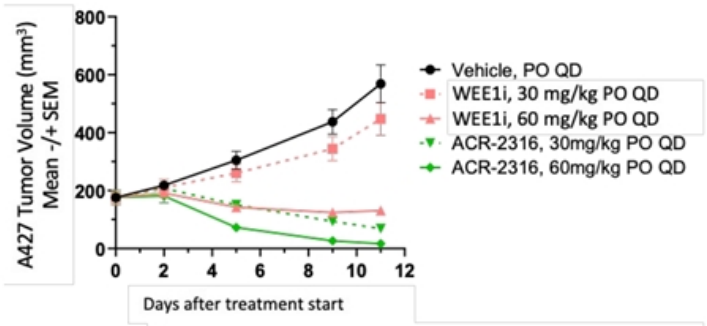


ACR-2316 DEMONSTRATES POTENT MONOTHERAPY ANTI-TUMOR ACTIVITY IN TUMOR-BEARING MICE

ACR-2316 anti-tumor activity (QDx7; PO)



ACR-2316 anti-tumor activity (5d on/2d off; PO)



ACR-2316 causes tumor regression, in contrast to the highest tolerated doses of benchmark WEE1 and PKMYT1 inhibitors, which only result in tumor inhibition

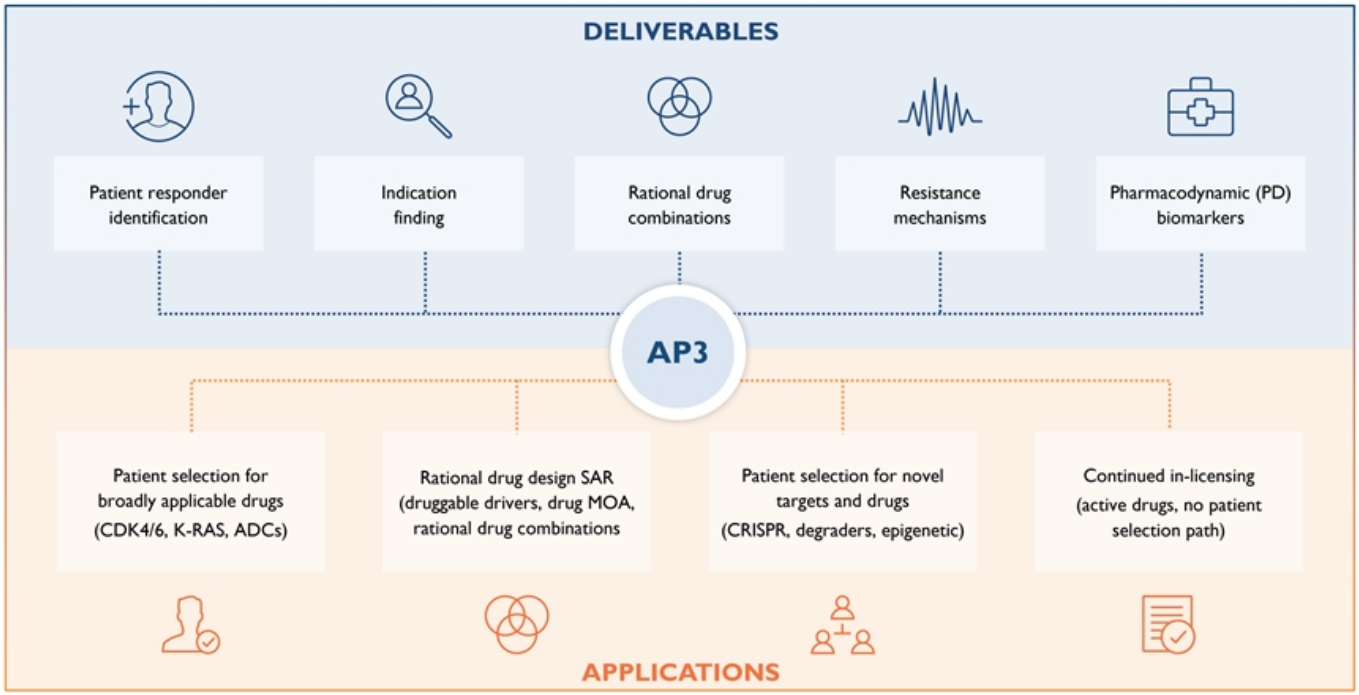
ACR-2316 FAVORABLE PRECLINICAL PROFILE

	Target	ACR-2316
MOA	• AP3 phosphoproteomics-based, optimized MOA; selective, dual WEE1/PKMYT1 inhibition	✓
Potency	• In vitro kinase activity, IC_{50} ≤ 10 nM • Potent target engagement in optimized ratio • Activity across sensitive human tumor cell lines, CC_{50} <100 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	✓ ✓

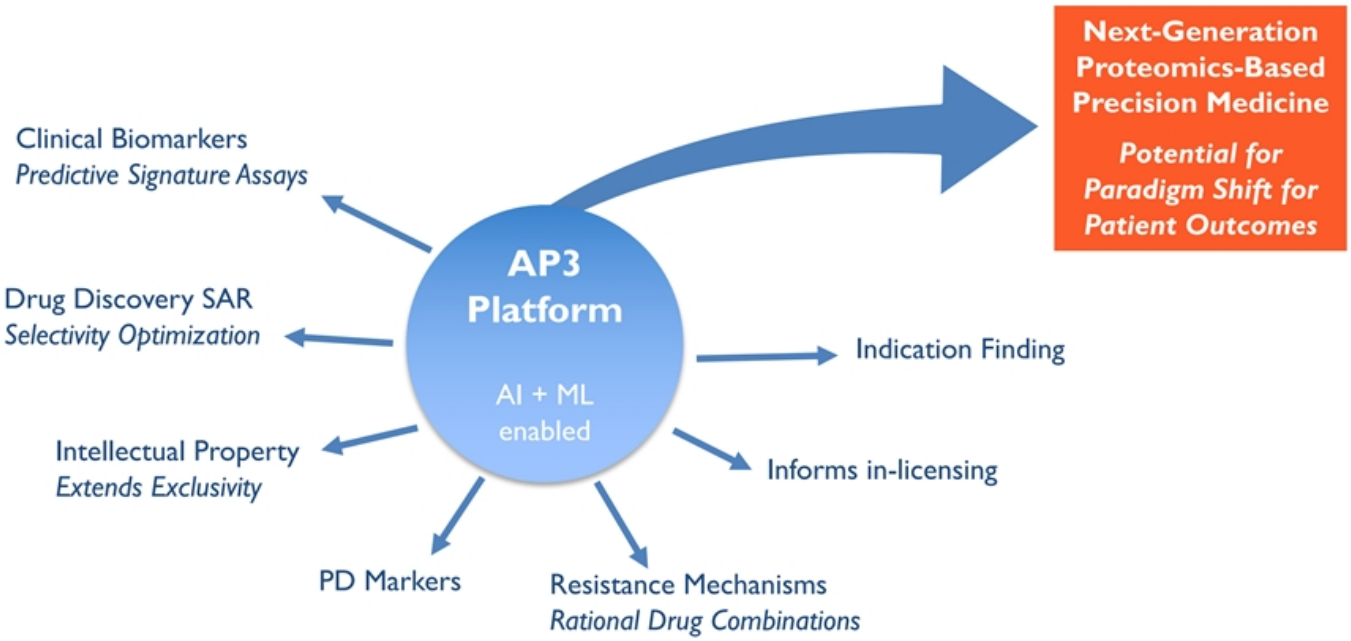
ACR-2316 DEVELOPMENT: NEXT STEPS

- Completion of IND-enabling studies
- ACR-2316 OncoSignature generation
- OncoSignature indication finding and prioritization for clinical development
- Planned IND filing Q4 2024, pending IND-enabling studies, in preparation for monotherapy clinical development with OncoSignature patient selection

AP3: BROAD APPLICABILITY AND UNTAPPED POTENTIAL



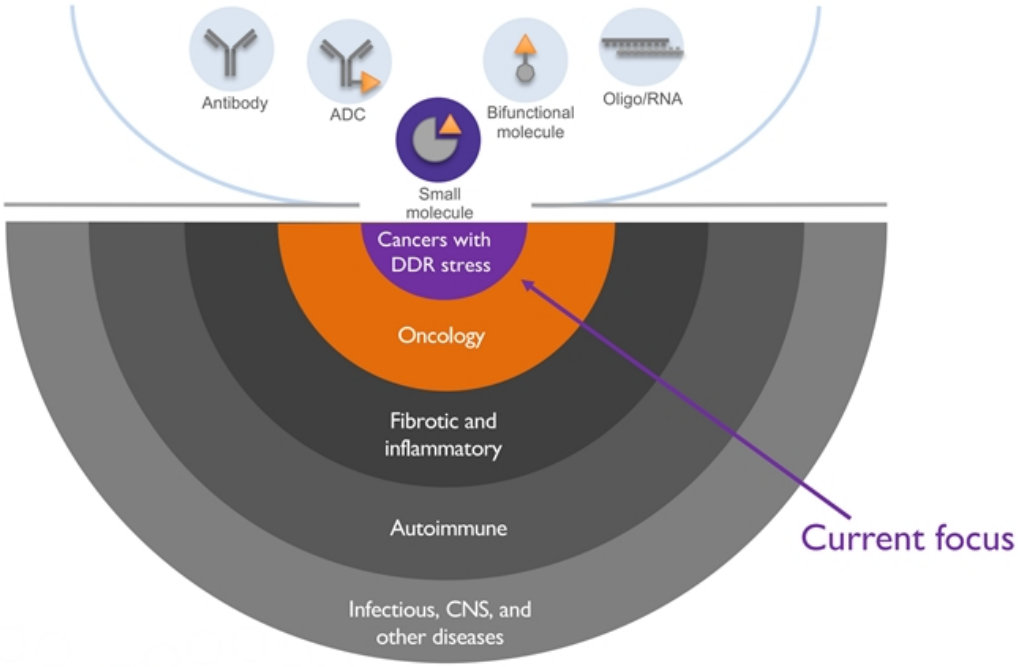
AP3 GENERATES VALUE ACROSS MULTIPLE DIMENSIONS



THE AP3 APPROACH IS MODALITY AND DISEASE AGNOSTIC

Therapeutic modalities

Therapeutic areas



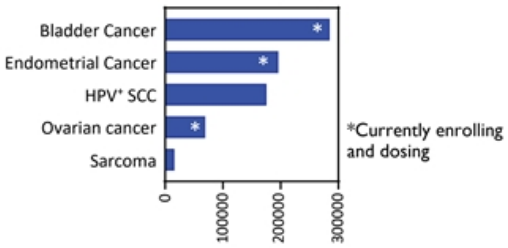
FINANCIAL HIGHLIGHTS AS OF Q2 2023

Cash and marketable securities	Projected runway into	Fully Diluted Shares Outstanding
$151.0M	2025	27.0M
Balance sheet 30-June-2023	Current operating plan, assuming no additional financing	Shares and equity grants outstanding 30-June-2023

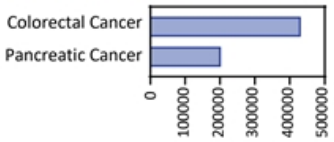
Unaudited.

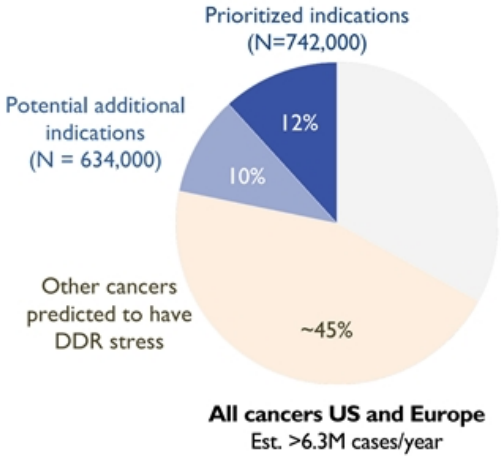
ACRIVON ADDRESSABLE MARKETS (US & EU INCIDENCE)

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

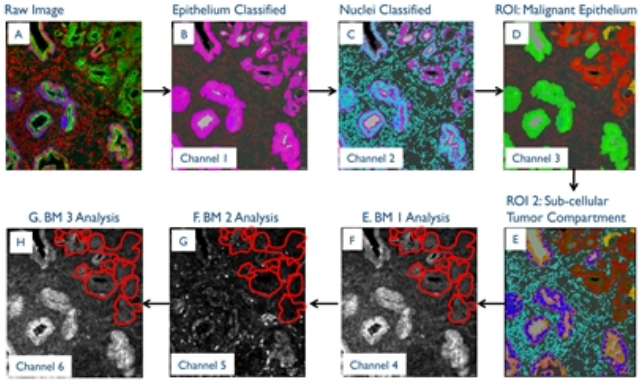
- ~30% (N = 223,000) of prioritized indications predicted sensitive to single agent ACR-368
- WEE1 and/or PKMYT1 inhibitor combinations with ACR-368 might further expand addressable fraction within sensitive tumor types

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)

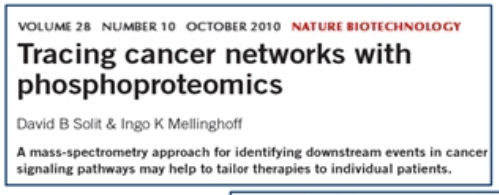
RESEARCH ARTICLE

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:

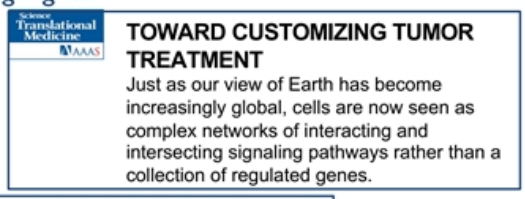


VOLUME 28 NUMBER 10 OCTOBER 2010 NATURE BIOTECHNOLOGY

Tracing cancer networks with phosphoproteomics

David B Solit & Ingo K Mellinghoff

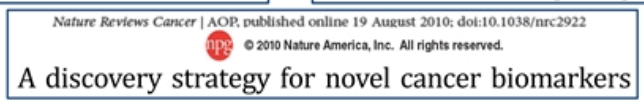
A mass-spectrometry approach for identifying downstream events in cancer signaling pathways may help to tailor therapies to individual patients.



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

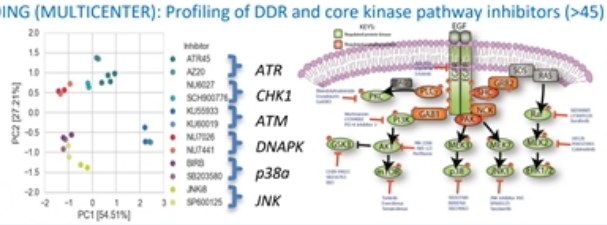
Spatial-proteomics reveals phospho-signaling dynamics at subcellular resolution

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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- Expert on protein biomarkers and quantitative tissue imaging
- Academic lead on ProMark®

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- Top 0.1% most cited scientist in protein sciences

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NCI Collaborator

Investigator, Lasker Clinical Research Scholar, NCI

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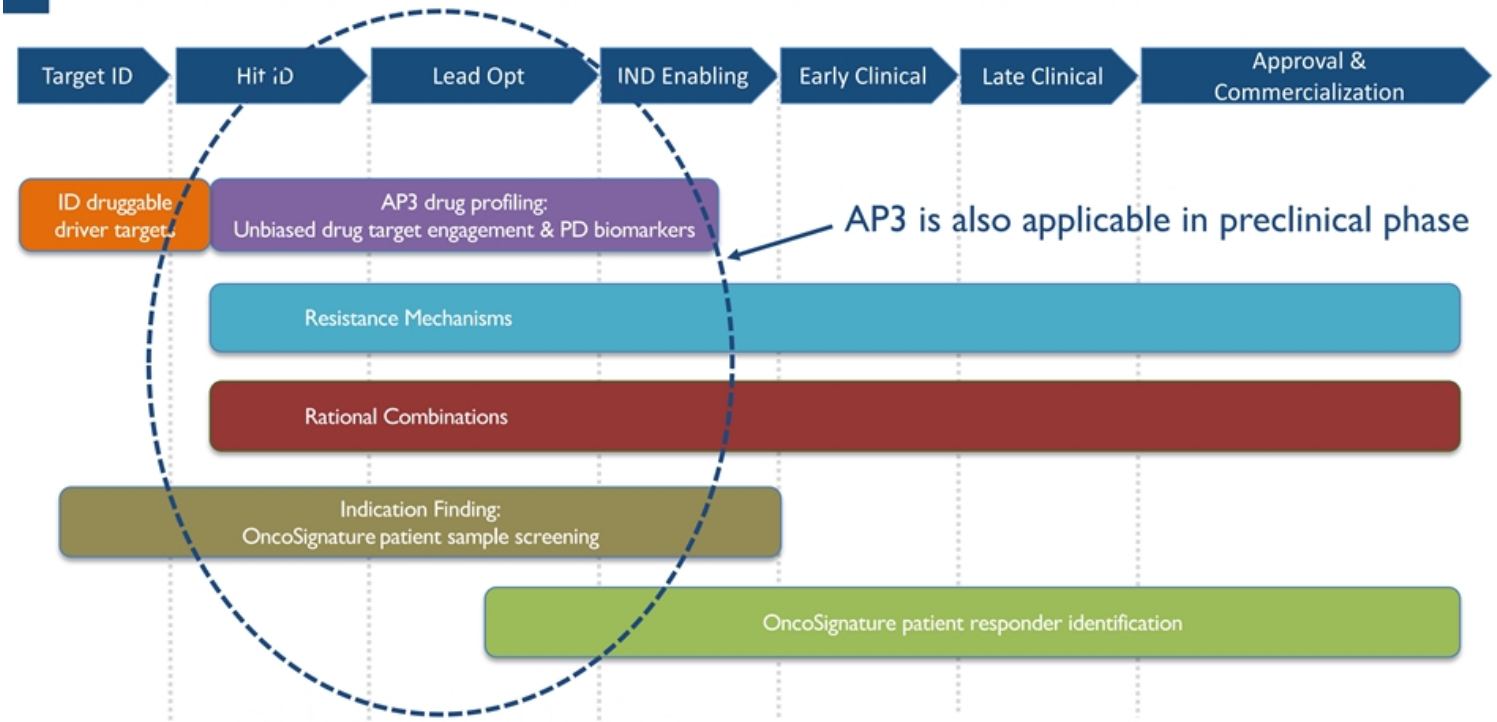
- Lead and co-PI on numerous HGSOC &TNBC trials
- Lead PI on ACR-368 platinum-resistant ovarian trials

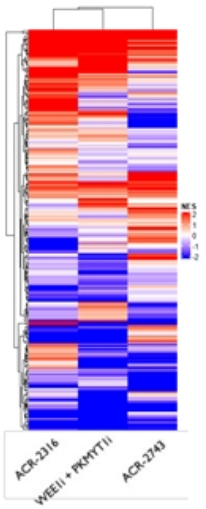
AP3 IS APPLICABLE ACROSS DRUG DEVELOPMENT STAGES



OPTIMIZED DUAL INHIBITORS SHOW SHARED AND DIFFERENTIATED PATHWAY EFFECTS

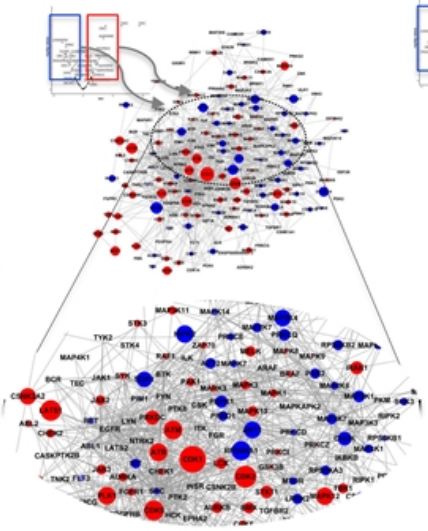
Optimized dual WEE1 and PKMYT1 inhibitors affect cell cycle and canonical MAPK pathways in desirable manner

Substrate motif-inferred kinase activities

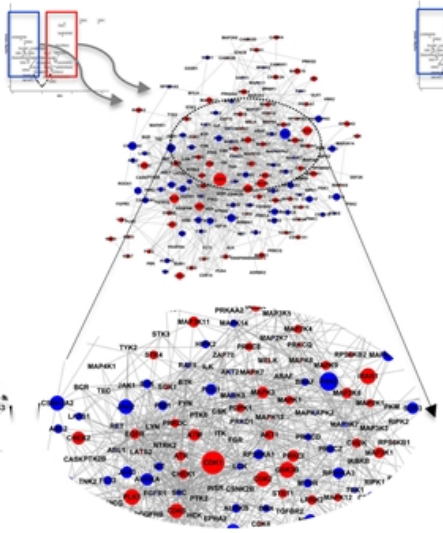


Kinase activity based on proprietary PTM-SEA-based hybrid workflow and analyses

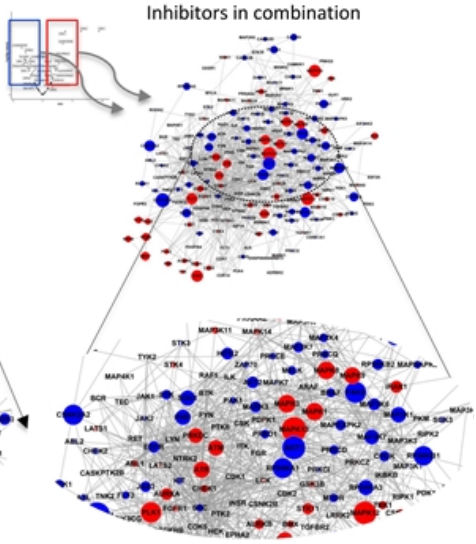
ACR-2316

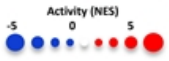


ACR-2743



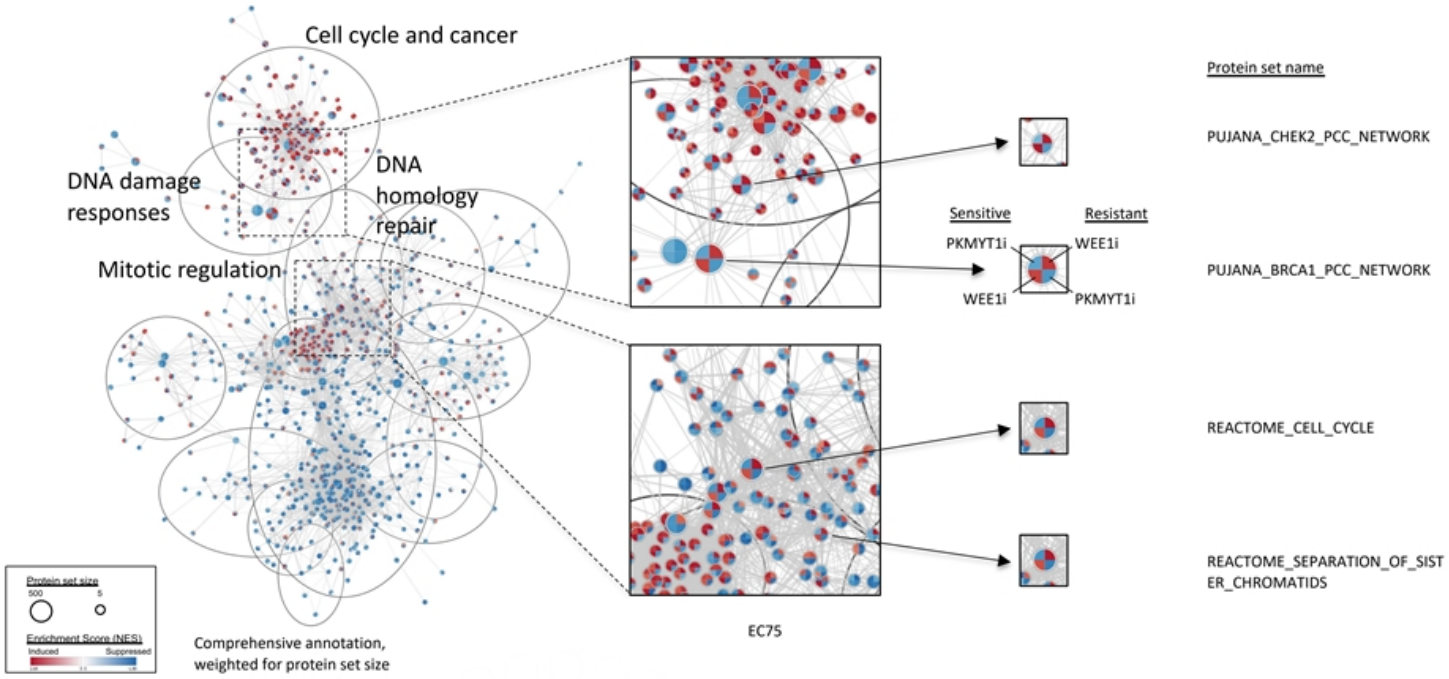
Benchmark* WEE1 + PKMYT1 Inhibitors in combination





*Clinical-stage selective WEE1 and PKMYT1 inhibitors

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



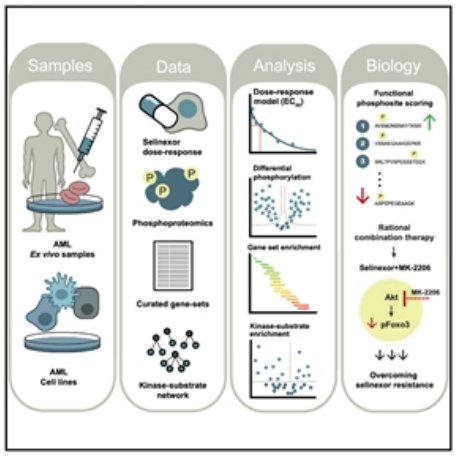
AP3 REVEALS SINGLE AGENT SENSITIVITY CONTEXT AND RATIONAL DRUG COMBINATIONS INDEPENDENT OF GENETIC INFORMATION

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