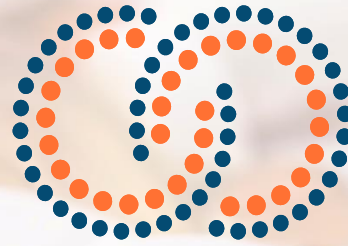


Acrivon

Therapeutics



*ACRIVON PREDICTIVE PRECISION PROTEOMICS (AP3)
OVERCOMING LIMITATIONS OF GENETICS-BASED PRECISION MEDICINE*

CORPORATE PRESENTATION

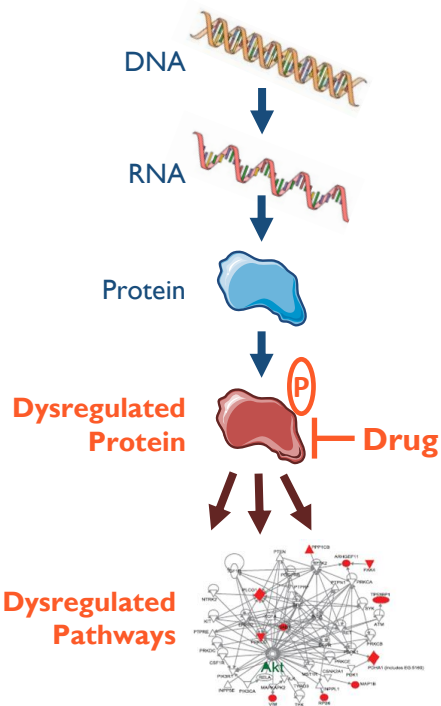
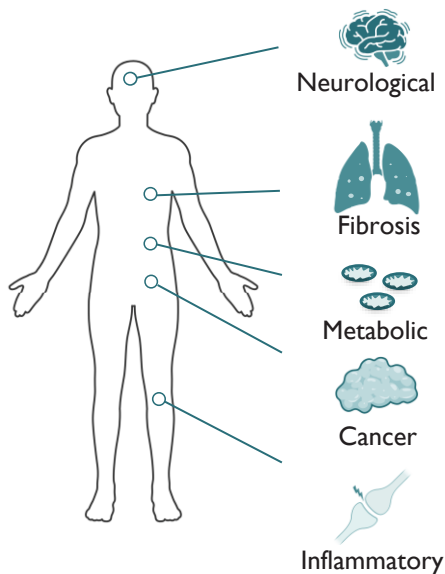
DECEMBER 2024

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.

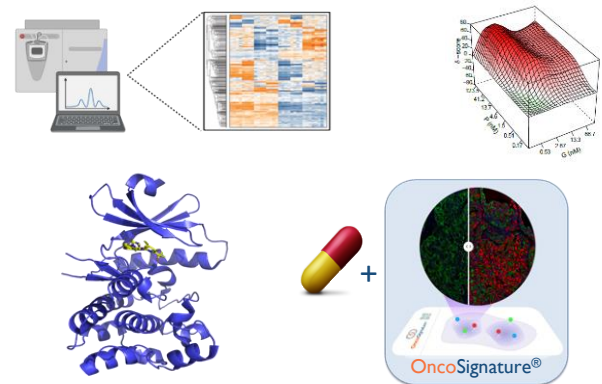
You are cautioned not to place undue reliance on these forward-looking statements, which are made only as of the date of this presentation. We undertake no obligation to update any forward-looking statements or to reflect new information or the occurrence of unanticipated events, except as required by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

ACRIVON THERAPEUTICS – A NEXT-GENERATION PRECISION MEDICINE COMPANY



Acrivon Predictive Precision Proteomics (AP3)

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



Blume-Jensen, P & Hunter, T: Oncogenic kinase signaling *Nature* (2001)

Olsen, JV et al: Global, in vivo, and site-specific phosphorylation dynamics in signaling networks *Cell* (2006);

Andersen, JN et al: Pathway-based identification of biomarkers for targeted therapeutics: personalized oncology with PI3K pathway inhibitors *Sci Transl Med* (2010)

ACRIVON THERAPEUTICS FOUNDATION

Development Site (Boston)

- Drug development and clinical biomarkers
- ML/AI-driven AP3 analyses
- Clinical leadership and trial oversight

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



Peter Blume-Jensen,
MD, PhD
CEO, President,
Co-Founder
Inventor of AP3



Kristina Masson
PhD, MBA
EVP, Bus Ops,
Lund Site Head
Co-Founder



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

Precision-Proteomics Site (Lund/Copenhagen)

- Early pipeline drug programs
- BM identification and drug profiling
- Mass spectrometry

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



Founded 2018, IPO November 2022 (NASDAQ:ACRV)

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

ACCOMPLISHED LEADERSHIP TEAM



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

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



Rasmus Holm-Jorgensen
Chief Financial Officer

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



Kristina Masson, Ph.D., M.B.A.
Site Head Acrivon AB, Co-Founder
EVP Business Operations

- Cross-functional Leadership Merrimack Pharmaceuticals, MIT/BROAD
- Founder and CEO, OncoSignature AB (acquired by Acrivon Therapeutics)



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

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



Eric Devroe, Ph.D.
Chief Operating Officer

- Founder and CEO, Opsonix
- Business executive MD Anderson Cancer Center and Metamark
- EIR Wyss Institute, Harvard
- Associate, Flagship Pioneering



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

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



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

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

CRITICAL CHALLENGES FACING BIOPHARMA INDUSTRY

Challenge

Acrivon Predictive Precision Proteomics (AP3)



Discovering **potent** compounds suitable for **clinical monotherapy**

Optimal target/pathway selectivity for rapid generation of single agent active compounds



Determining **which patients will benefit from** those drugs

Identification of drug-sensitive indications and patients for actionable precision medicine



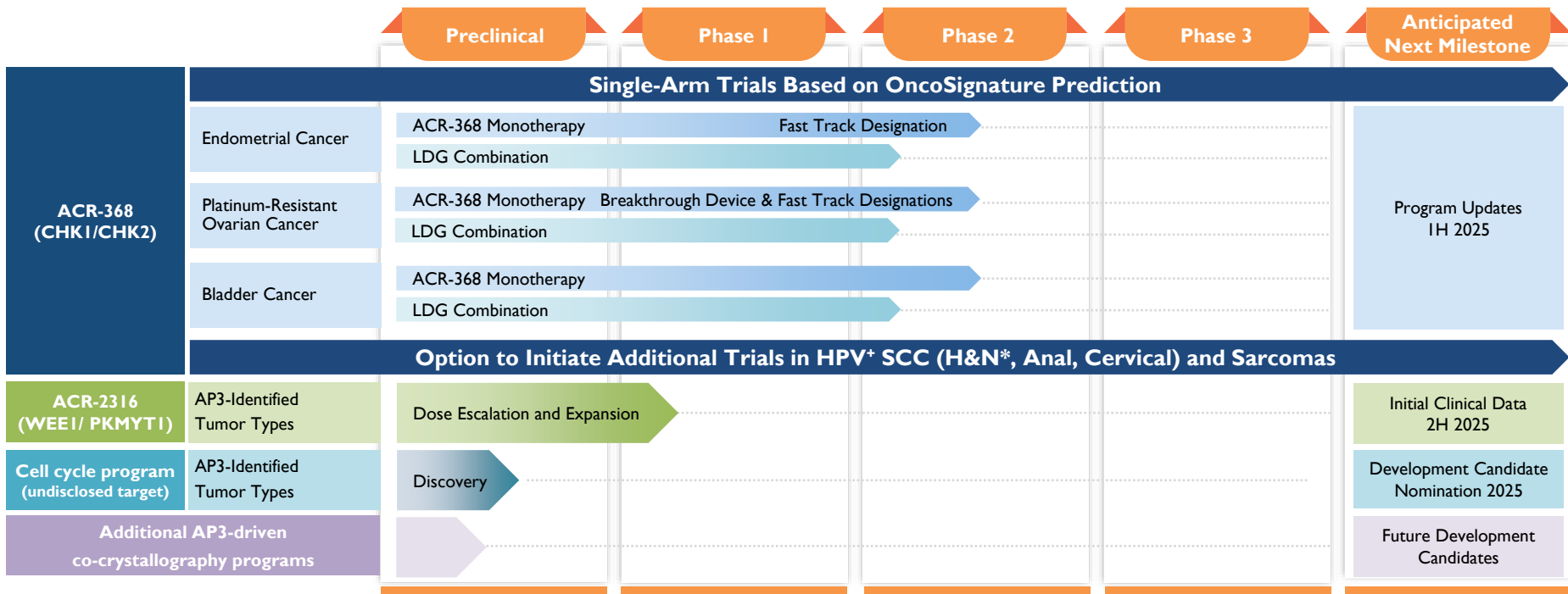
Preventing or reducing resistance to **maximize response durability**

Ability to rapidly identify and overcome resistance mechanisms



AP3 is a proprietary, machine learning-enabled internal R&D engine that effectively addresses these challenges, driving rapid advancement of our pipeline

ACRIVON PIPELINE



ACR-368 Monotherapy

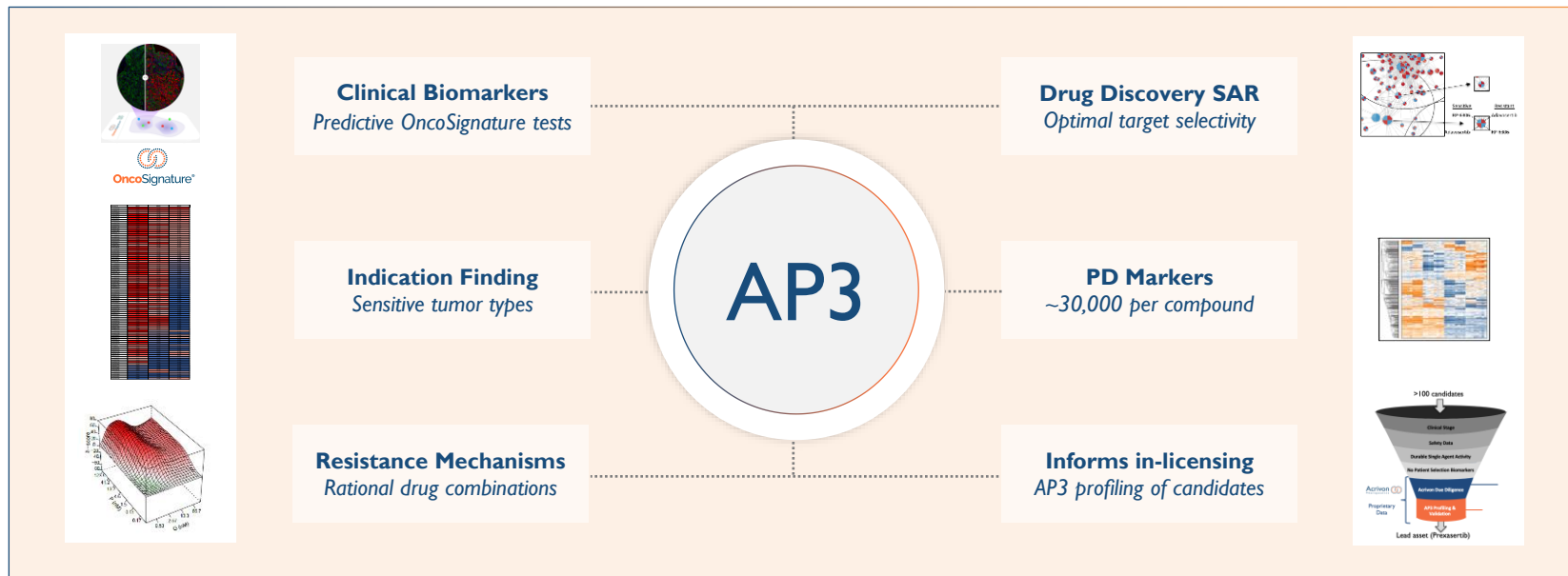
Registrational intent Phase 2 single arm trials based on predicted sensitivity to ACR-368 monotherapy in OncoSignature-positive patients

LDG Combination

Exploratory Phase 1b/2 single arm trials of ACR-368 in combination with low dose gemcitabine, or LDG, in OncoSignature-negative patients

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

AP3-BASED DRUG DISCOVERY AND CLINICAL DEVELOPMENT IN PREDICTED SENSITIVE SUBJECTS AND TUMOR TYPES

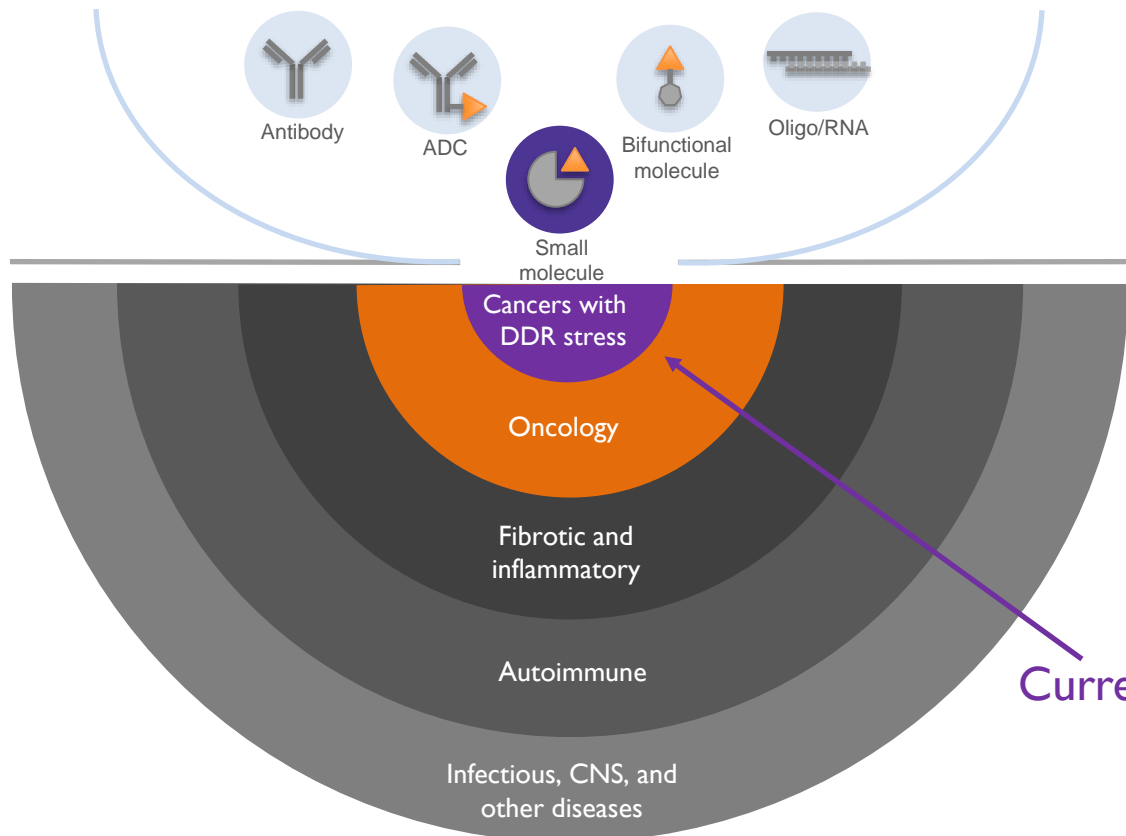


Streamlined Clinical Development
Predicted sensitive indications with informed dose optimization



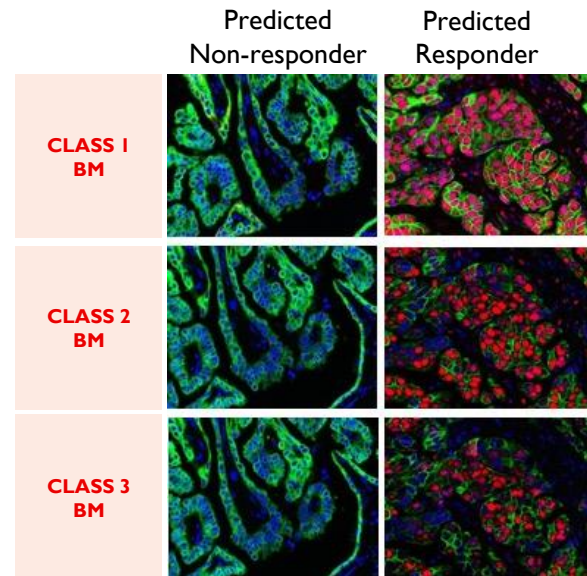
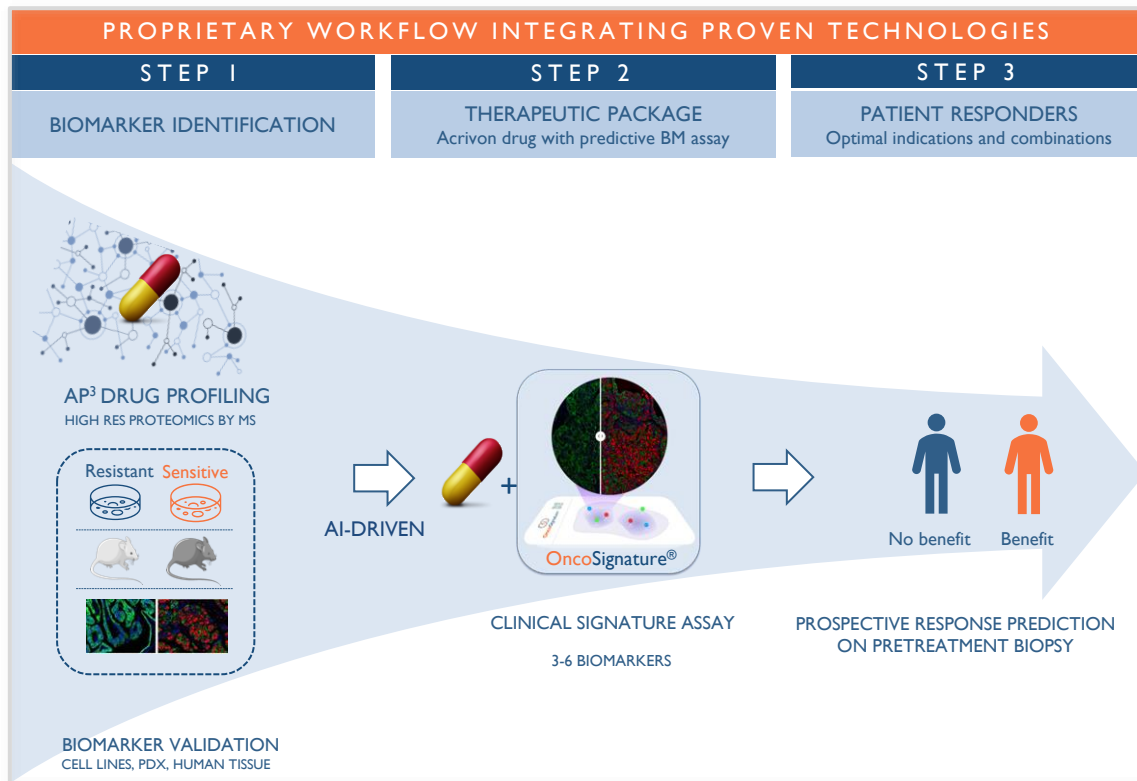
THE AP3 APPROACH IS MODALITY AND DISEASE AGNOSTIC

Therapeutic modalities



Current focus

AP3 PLATFORM: DRUG RESPONSE PREDICTION IN INDIVIDUAL PATIENTS

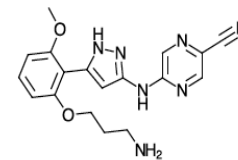


Patients without biomarkers critical for drug sensitivity efficiently excluded

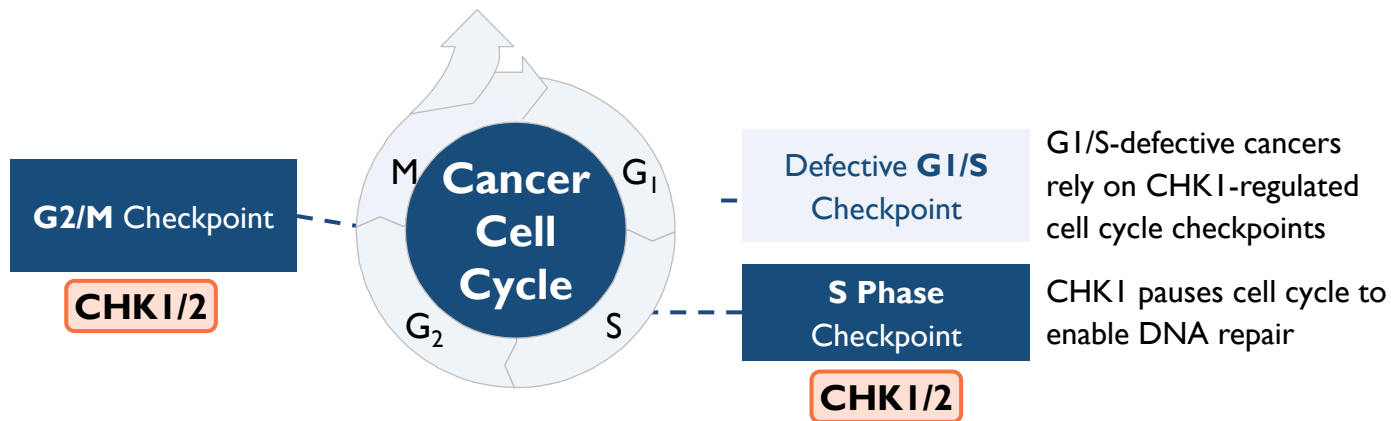
"Disease Pathway-Based Method to Generate Biomarker Panels Tailored to Specific Therapeutics for Individualized Treatments": EP 2 229 589, issued June 10, 2015; US2017/0067877A9, pending. OncoSignature® is a Registered Trademark: US Reg. No. 5,718,472; Int. Cl. 5, 42. Intl. Reg. 1382289

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

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



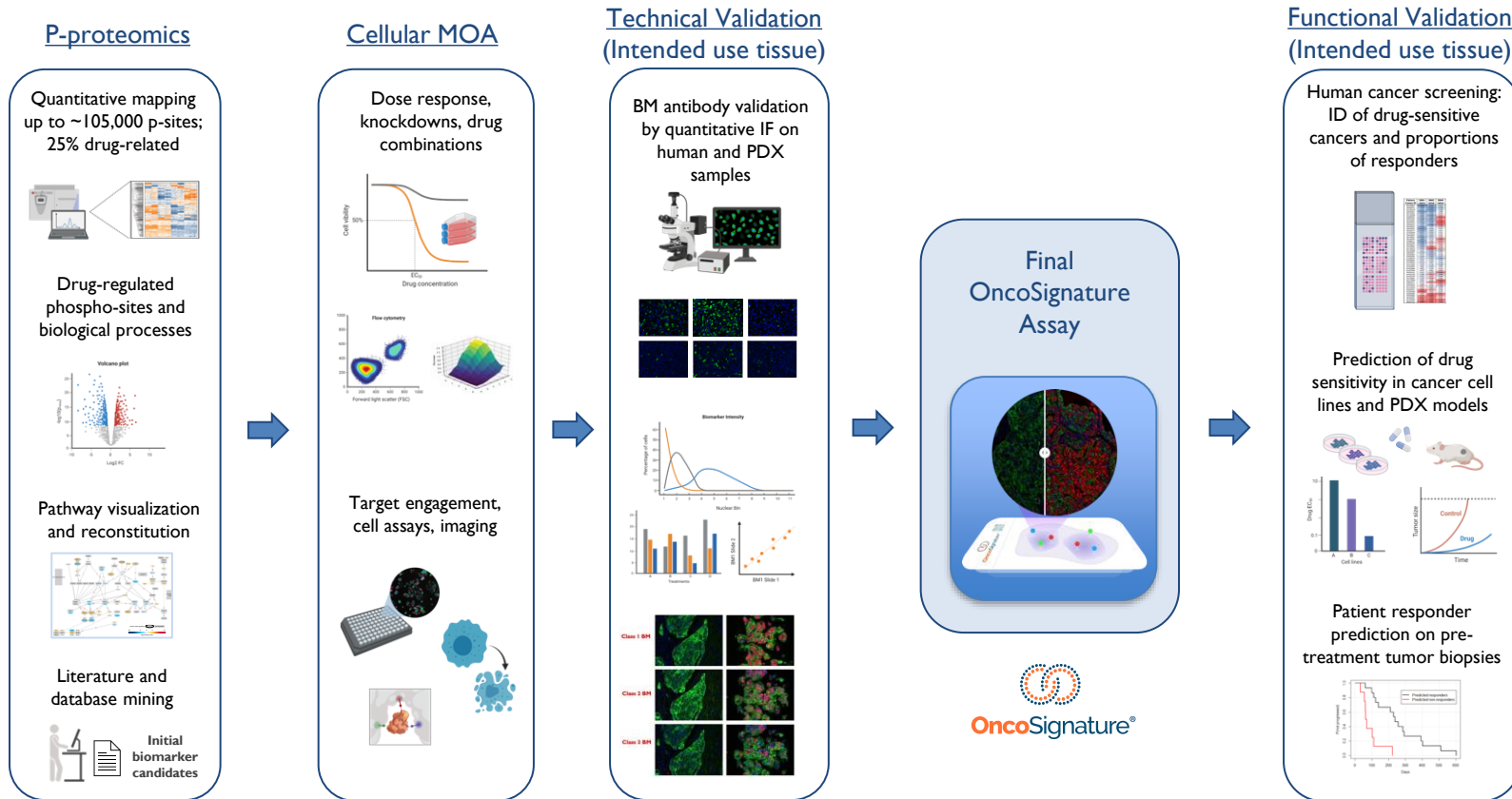
ACR-368 (MW): 365.4



DRUG TARGET PROFILE AT TIME OF IN-LICENSING

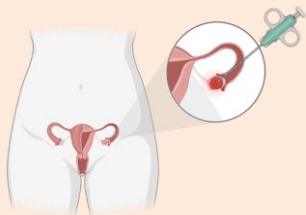
- **Durable monotherapy activity:** Platinum-resistant ovarian and squamous cell cancers (Anal and H&N)
- **Large safety database, favorable safety profile:** >1,000 patients treated (~50% mono, ~50% in combination)
- **Ideal for AP3 method:** Proven clinical activity, but requires patient responder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

DEVELOPMENT OF AP3-BASED PATIENT SELECTION ONCOSIGNATURE TESTS



ACR-368 ONCOSIGNATURE TEST: USAGE IN THE CLINIC

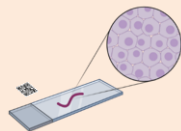
Pretreatment tumor biopsy



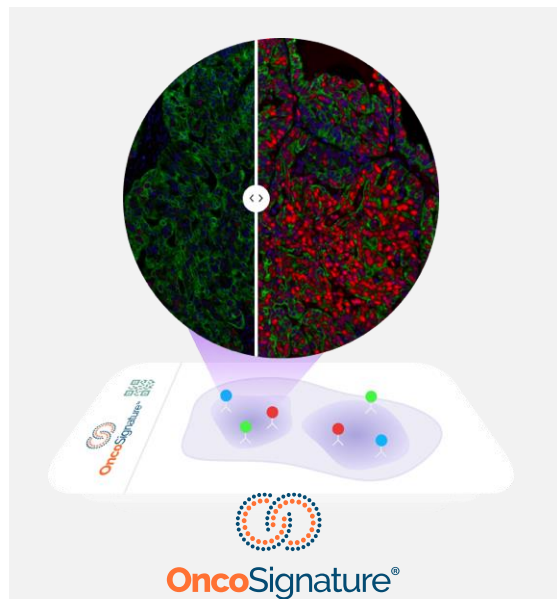
Routine FFPE processing



Biopsy in
FFPE
block



Automated tumor
Region-of-Interest
biomarker scoring



Treatment decision based on patient stratification



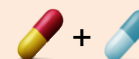
OncoSignature-
positive



OncoSignature-
negative



ACR-368
monotherapy

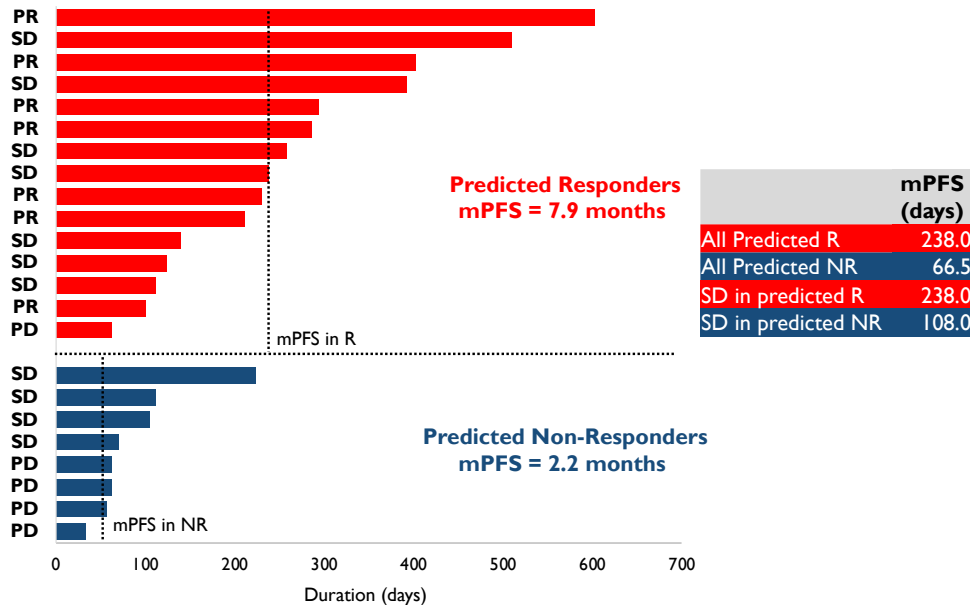
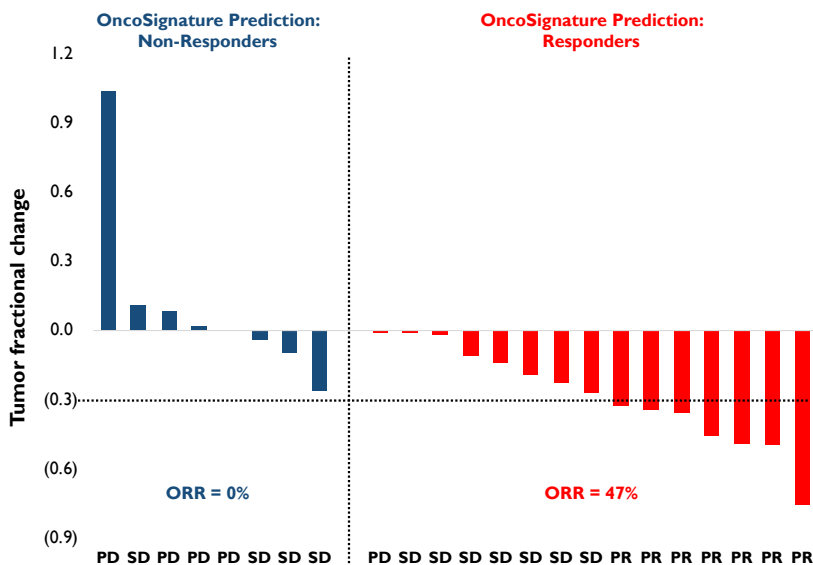


ACR-368 + LDG
combination

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

BIOPSY STUDY I: 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**



Result: ORR ~47%; mPFS = 7.9 months

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

HGS Ovarian

Tissue ID	BM1	BM2	BM3
Rho00179	0.04	0.04	0.14
Rho00180	0.04	0.04	0.14
Rho00181	0.13	0.10	0.20
Rho00182	0.04	0.14	0.20
Rho00183	0.04	0.04	0.14
Rho00184	0.04	0.04	0.14
Rho00185	0.04	0.04	0.14
Rho00186	0.04	0.04	0.14
Rho00187	0.04	0.04	0.14
Rho00188	0.04	0.04	0.14
Rho00189	0.04	0.04	0.14
Rho00190	0.04	0.04	0.14
Rho00191	0.04	0.04	0.14
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Rho00230	0.04	0.04	0.14
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Rho00248	0.04	0.04	0.14
Rho00249	0.04	0.04	0.14
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Rho00252	0.04	0.04	0.14
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Rho00280	0.04	0.04	0.14
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Rho00282	0.04	0.04	0.14
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Rho00285	0.04	0.04	0.14
Rho00286	0.04	0.04	0.14
Rho00287	0.04	0.04	0.14
Rho00288	0.04	0.04	0.14
Rho00289	0.04	0.04	0.14
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Rho00293	0.04	0.04	0.14
Rho00294	0.04	0.04	0.14
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Rho00296	0.04	0.04	0.14
Rho00297	0.04	0.04	0.14
Rho00298	0.04	0.04	0.14
Rho00299	0.04	0.04	0.14
Rho00300	0.04	0.04	0.14

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

Sq. NSCLC

Tissue ID	BM1	BM2	BM3
Rho20122	0.17	0.26	0.02
Rho20099	0.06	0.06	0.06
Rho20029	0.48	0.28	0.00
Rho20005	0.34	0.06	0.00
Rho10095	0.28	0.02	0.00
Rho20051	0.11	0.01	0.14
Rho20067	0.14	0.03	0.00
Rho20284	0.09	0.00	0.00
Rho20141	0.05	0.18	0.00
Rho20032	0.05	0.01	0.00
Rho10199	0.05	0.06	0.03
Rho20097	0.04	0.00	0.00
Rho20250	0.04	0.00	0.00
Rho20190	0.04	0.00	0.00
Rho20243	0.02	0.00	0.01
Rho20012	0.02	0.41	0.07
Rho20148	0.02	0.05	0.06
Rho20006	0.01	0.00	0.02
Rho20296	0.01	0.00	0.00
Rho20186	0.01	0.02	0.02
Rho20166	0.01	0.05	0.01
Rho20208	0.01	0.01	0.00
Rho20237	0.01	0.00	0.00
Rho20343	0.01	0.00	0.01
Rho20233	0.01	0.04	0.06
Rho20007	0.00	0.26	0.08
Rho20138	0.00	0.01	0.01
Rho20231	0.00	0.00	0.01
Rho20231	0.00	0.00	0.01
Rho20231	0.00	0.00	0.01
Rho20088	0.00	0.00	0.00
Rho20168	0.00	0.18	0.00
Rho20164	0.00	0.00	0.00
Rho20301	0.00	0.18	0.00
Rho20083	0.00	0.00	0.00
Rho20086	0.00	0.00	0.00
Rho20163	0.00	0.00	0.00
Rho20096	0.00	0.00	0.00
Rho20140	0.00	0.00	0.00
Rho20302	0.00	0.00	0.00
Rho20213	0.00	0.00	0.00
Rho20311	0.00	0.00	0.00
Rho20252	0.00	0.00	0.00
Rho20415	0.00	0.00	0.00
Rho20298	0.00	0.00	0.00
Rho10086	0.00	0.00	0.00
Rho20261	0.00	0.11	0.00
Rho20383	0.00	0.01	0.06
Rho20386	0.00	0.03	0.00
Rho20248	0.00	0.00	0.00
Rho20221	0.00	0.00	0.00
Rho20184	0.00	0.00	0.01
Rho20119	0.00	0.00	0.05
Rho20380	0.00	0.00	0.02
Rho20244	0.00	0.00	0.00
Rho20274	0.00	0.00	0.00
Rho20227	0.00	0.00	0.00
Rho10079	0.00	0.03	0.00
Rho20282	0.00	0.00	0.00
Rho20249	0.00	0.00	0.00
Rho20255	0.00	0.00	0.00

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

Bladder cancer

Tissue ID	BM1	BM2	BM3
Ubd040112	0.69	0.48	0.65
Ubd040016	0.30	0.58	0.63
Ubd040039	0.43	0.33	0.54
Ubd030040	0.88	0.73	0.45
Ubd040287	0.63	0.34	0.40
Ubd040151	0.65	0.72	0.34
Ubd040225	0.76	0.64	0.33
Ubd040282	0.27	0.16	0.26
Ubd060279	0.29	0.13	0.16
Ubd030229	0.79	0.39	0.15
Ubd040104	0.84	0.58	0.15
Ubd040056	0.79	0.83	0.14
Ubd070017	0.62	0.40	0.14
Ubd040204	0.12	0.76	0.12
Ubd040111	0.91	0.81	0.10
Ubd040142	0.84	0.62	0.09
Ubd030138	0.54	0.11	0.09
Ubd040043	0.65	0.92	0.08
Ubd050077	0.72	0.46	0.08
Ubd020464	0.73	0.63	0.07
Ubd040177	0.69	0.84	0.04
Ubd040214	0.29	0.17	0.03
Ubd040128	0.77	0.29	0.03
Ubd050035	0.17	0.33	0.02
Ubd080024	0.18	0.28	0.01
Ubd040101	0.26	0.31	0.01
Ubd030151	0.79	0.61	0.00
Ubd040398	0.35	0.40	0.00
Ubd040008	0.75	0.90	0.00
Ubd040162	0.87	0.10	0.00
Ubd040341	0.19	0.09	0.03
Ubd070027	0.20	0.08	0.01
Ubd040030	0.96	0.07	0.01
Ubd040067	0.61	0.06	0.03
Ubd040074	0.80	0.03	0.10
Ubd040218	0.85	0.02	0.15
Ubd040055	0.07	0.03	0.02
Ubd040050	0.06	0.58	0.00
Ubd020068	0.05	0.11	0.18
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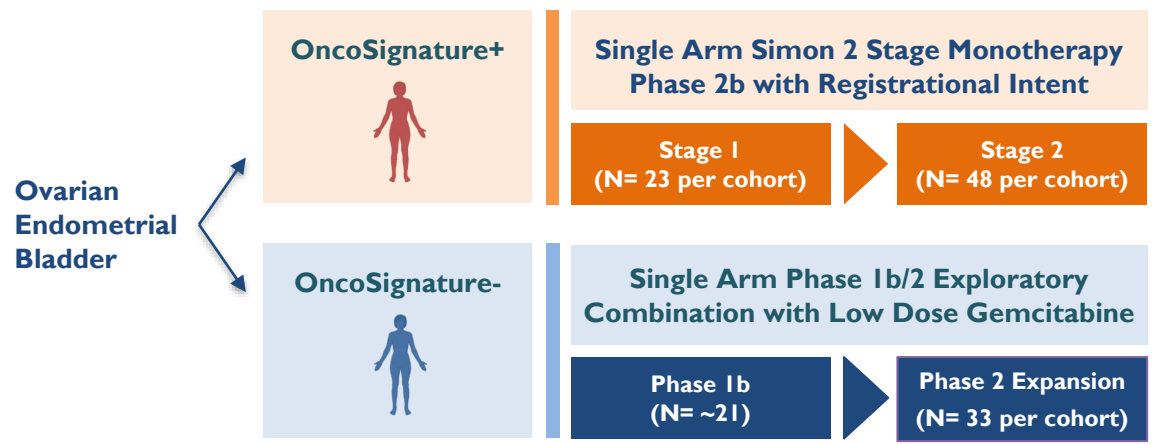
OncoSignature-positive = 30-50%

Endometrial cancer

Tissue ID	BM1	BM2	BM3
Fur021904	0.16	0.38	0.99
Fur021989	0.06	0.17	0.71
Fur021785	0.14	0.55	0.63
Fur021984	0.87	0.62	0.68
Fur021937	0.81	0.65	0.61
Fur020367	0.12	0.22	0.54
Fur020368	0.85	0.68	0.68
Fur020113	0.90	0.56	0.31
Fur020288	0.60	0.26	0.30
Fur020281	0.21	0.57	0.27
Fur130010	0.79	0.75	0.27
Fur021791	0.75	0.31	0.26
Fur140135	0.12	0.35	0.25
Fur150643	0.61	0.73	0.22
Fur021558	0.61	0.33	0.22
Fur020131	0.73	0.57	0.18
Fur021367	0.30	0.55	0.18
Fur020506	0.68	0.48	0.17
Fur020163	0.23	0.33	0.12
Fur130009	0.18	0.69	0.10
Fur021197	0.35	0.70	0.09
Fur020587	0.18	0.34	0.08
Fur140460	0.77	0.51	0.07
Fur021980	0.30	0.74	0.06
Fur020831	0.18	0.45	0.04
Fur020809	0.36	0.58	0.00
Fur030068	0.41	0.63	0.00
Fur030132	0.50	0.68	0.00
Fur021437	0.98	0.37	0.00
Fur021620	0.41	0.10	0.33
Fur020073	0.29	0.06	0.21
Fur020115	0.55	0.02	0.90
Fur020077	0.68	0.00	0.17
Fur020703	0.05	0.27	0.00
Fur021233	0.05	0.66	0.00
Fur021561	0.04	0.01	0.14
Fur020837	0.04	0.06	0.04
Fur020246	0.04	0.40	0.03
Fur020280	0.03	0.42	0.25
Fur030193	0.03	0.10	0.02
Fur021641	0.02	0.30	0.01
Fur020121	0.02	0.	

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

- ACR-368 dosed at RP2D based on predicted sensitivity using our ACR-368 OncoSignature Assay run by our CDx partner
- 68 sites activated¹
- 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>

ENDOMETRIAL CANCER IS AN AP3-PREDICTED TUMOR TYPE

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



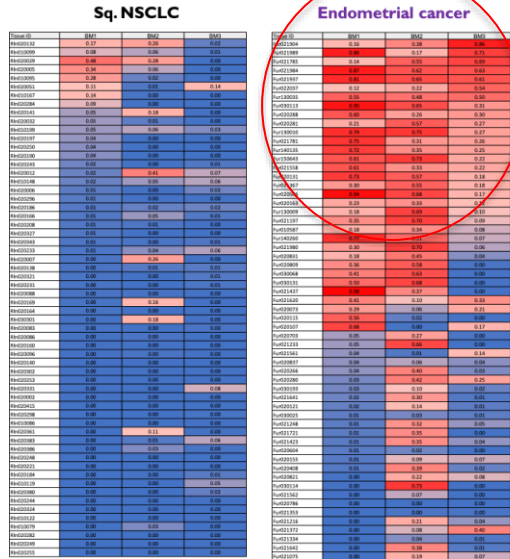
ACR-368 OncoSignature imaging demonstrates addition to CHK1/2 DDR axis



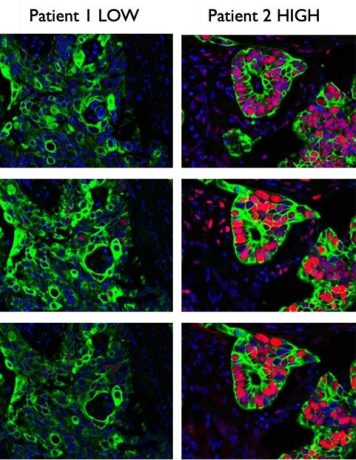
Confirmation of predicted sensitivity in genetically non-modified PDX models



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



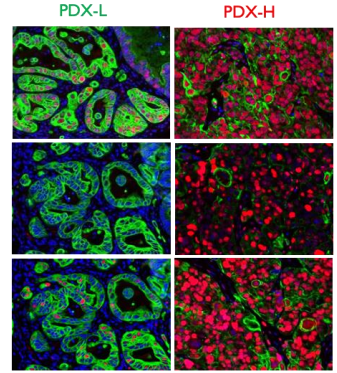
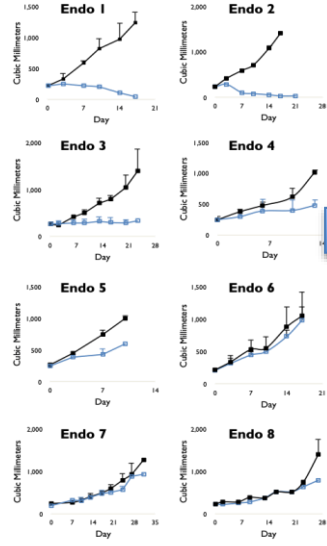
Endometrial patient samples



Predicted Non-Responders Predicted Responders



Endometrial PDX

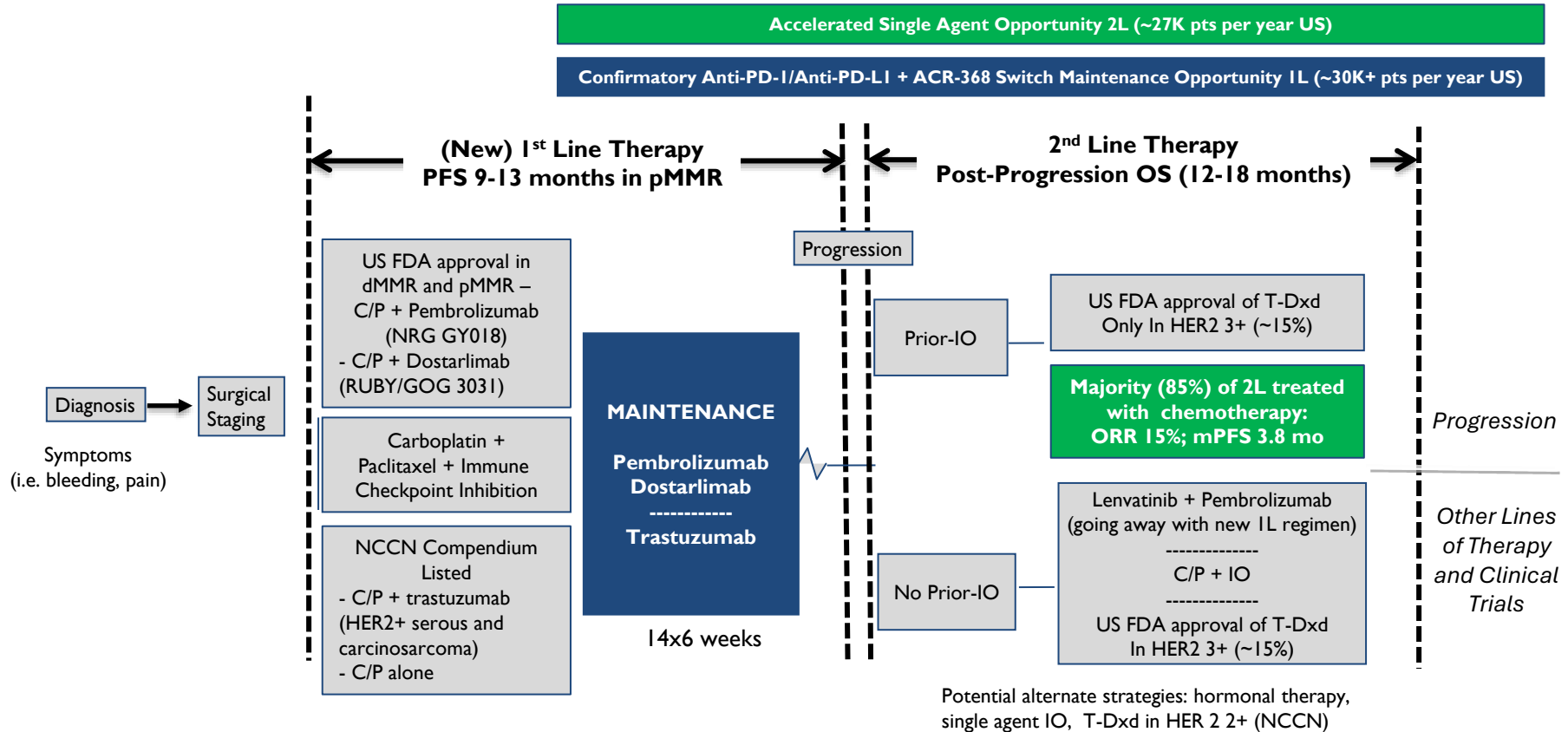


Predicted Non-Responders Predicted Responders

OncoSignature-positive = 0% (ORR in past trial: 0%) OncoSignature-positive = 30-40%

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

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



Adapted from Dr. R. Eskander

HIGH GRADE ADVANCED STAGE ENDOMETRIAL CANCER POTENTIAL FOR ACCELERATED APPROVAL $\geq 2^{\text{ND}}$ LINE (POST ANTI-PD-1)

ACR-368 Target Indication:

- High grade, locally advanced or metastatic, recurrent endometrial cancer
- Significant unmet need, attractive commercial potential
- Must have recurred after prior chemo and PD-1/PD-L1 inhibitor therapy¹
- Irrespective of molecular (MMR, p53, other) alterations and subtype (serous, endometrioid, clear cell, carcinosarcoma)

SOC:

- $\geq 2^{\text{nd}}$ line (post-PD-1 + chemo) ~14.7% ORR, mPFS 3.8 months²; patients in the control arm were not previously treated with anti-PD-1 therapy, only platinum, thus potentially overestimating the 2nd line ORR
- $\geq 3^{\text{rd}}$ line ~9% ORR, mPFS 2.8 months³

ACR-368 Target Product Profile:

- $\geq 25\%$ ORR with CI lower bound $>20\%$; mDoR ≥ 5.5 months

¹Unless ineligible for PD-1/PD-L1 therapy

²Eskander R et al, NEJM, 2023; Mirza MR et al, NEJM, 2023; Makker V et al, NEJM, 2022

³Ray-Coquard I et al, BJC, 2013

SIGNIFICANT ACR-368 ENDOMETRIAL PATIENT RESPONDER ENRICHMENT IN EFFICACY-EVALUABLE SUBJECTS¹ (N=23) IN REGISTRATIONAL INTENT PHASE 2 TRIAL

Meaningful positive data maturation since April R&D Event²

- **Prospective initial validation of the AP3-based ACR-368 OncoSignature now achieved for endometrial cancer (P = 0.009 vs P = 0.083)**
- **Confirmed ORR in BM+ subjects now 62.5% with the lower bound of 95% C.I. 30.4% (vs. 22.9%)**
- **Confirmed ACR-368 responders still on therapy; mDoR not yet reached (~6 months at time of data-cut vs ~2 months)**

Endometrial Cancer (data cut 25 July 2024)			
Overall Response	BM+ Monotherapy	BM-LDG Combination	Total
	N = 8	N = 15	N=23
	N (%)	N (%)	N (%)
CR	0 (0)	1 (7)	1 (4)
cPR	5 (63)	0 (0)	5 (22)
uPR	0 (0)	1 (7)	1 (4)
SD	1 (13)	6 (40)	7 (30)
PD	2 (25)	7 (47)	9 (39)
cORR (95% CI)	62.5% (30.4, 86.5)	6.7% (0.84, 31.8)	26% (12.3, 46.8)
OncoSignature BM+ vs BM-Segregation P = 0.009			

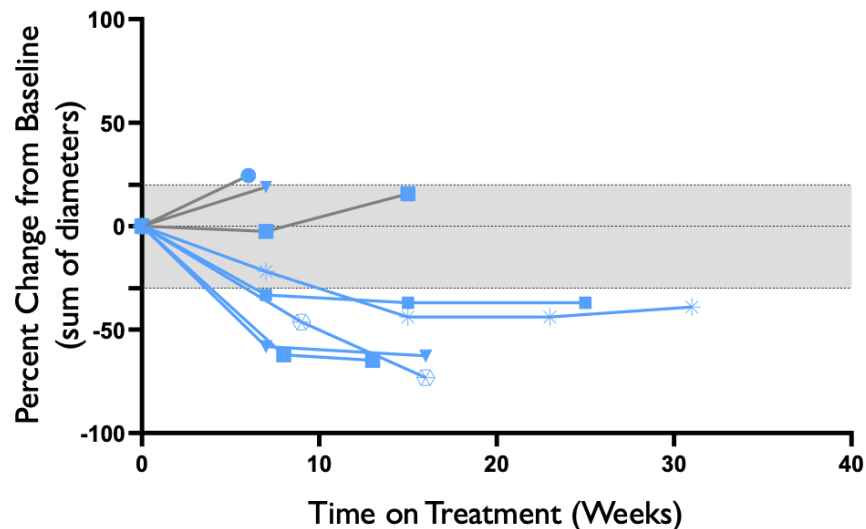
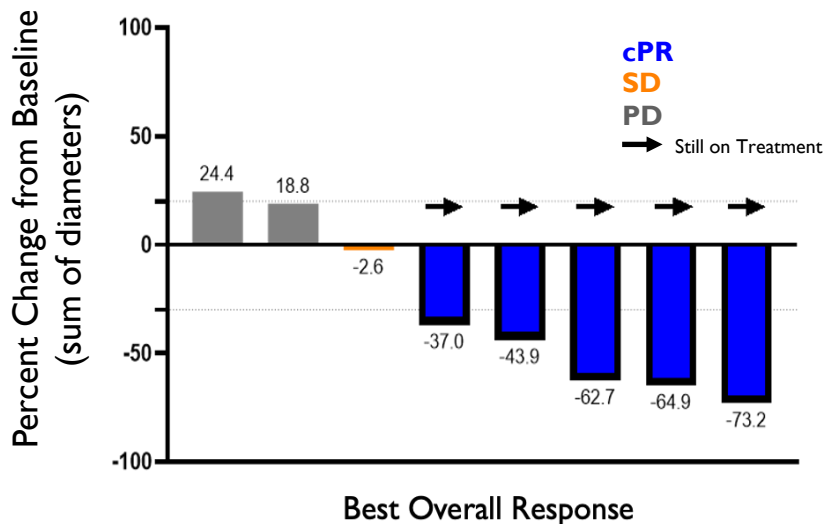
¹Subjects with ≥1 on-treatment scan

²<https://ir.acrivos.com/news-events/events-presentations>

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

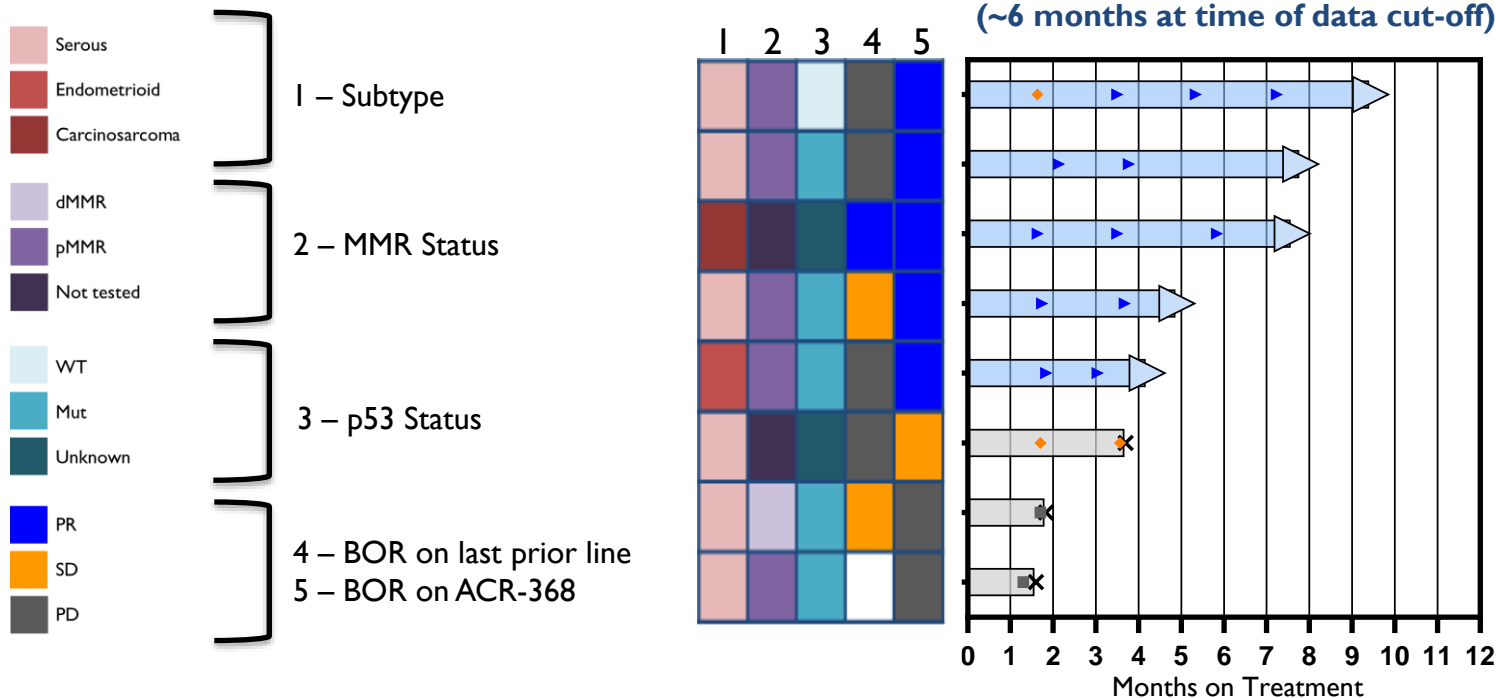
Confirmed ORR = 62.5%
95% C.I. (30.4%, 86.5%)

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



Data cut as of 25 July 2024, includes all BM+ subjects

ONGOING CONFIRMED RESPONSES IN BM+ ENDOMETRIAL SUBJECTS ACROSS SUBTYPES



- Durable responses in patients who all progressed on prior anti-PD-1 and whose BOR in last prior line was mostly PD
- Most patients are pMMR and p53 mutant, consistent with their prevalence in high grade endometrial cancer
- ACR-368 OncoSignature prediction is independent of molecular (incl. MMR) and histological subtype

Data current as of 25July2024

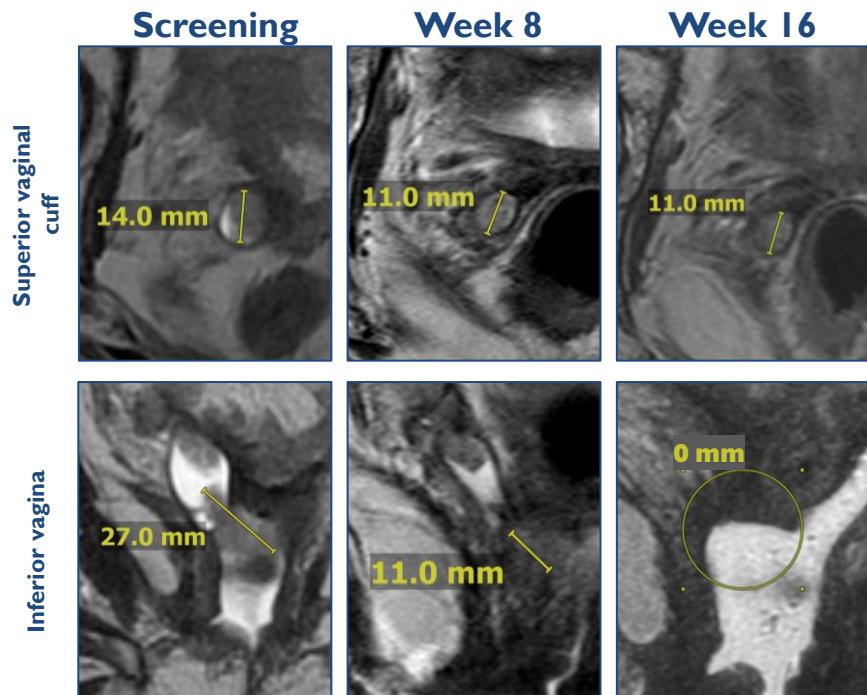
CONFIRMED RESPONSES IN ENOMETRIAL SUBJECTS WHO ALL PROGRESSED ON PRIOR ANTI-PD-I

Endometrial subtype	# Prior Lines	Last Prior Therapy (LPT)	BOR on LPT	BOR on ACR-368
Serous	3	Pembrolizumab/Lenvatinib	PD	cPR
Serous	2	Pembrolizumab/Lenvatinib	PD	cPR
Endometrioid	4	Cisplatin	PD	cPR
Serous	1	Pembrolizumab	SD	cPR
Carcinosarcoma	2	Pembrolizumab/Lenvatinib	PR	cPR
Serous	4	Liposomal doxorubicin	PD	SD
Serous	3	Pembrolizumab/Lenvatinib	<i>UNK</i>	PD
Serous	3	Pembrolizumab/Lenvatinib	<i>NA</i>	PD

- All confirmed responders progressed on prior PD-I therapy and majority had BOR = PD on last prior line of therapy
- Only 1 RECIST response amongst 6 patients with BOR data from LPT

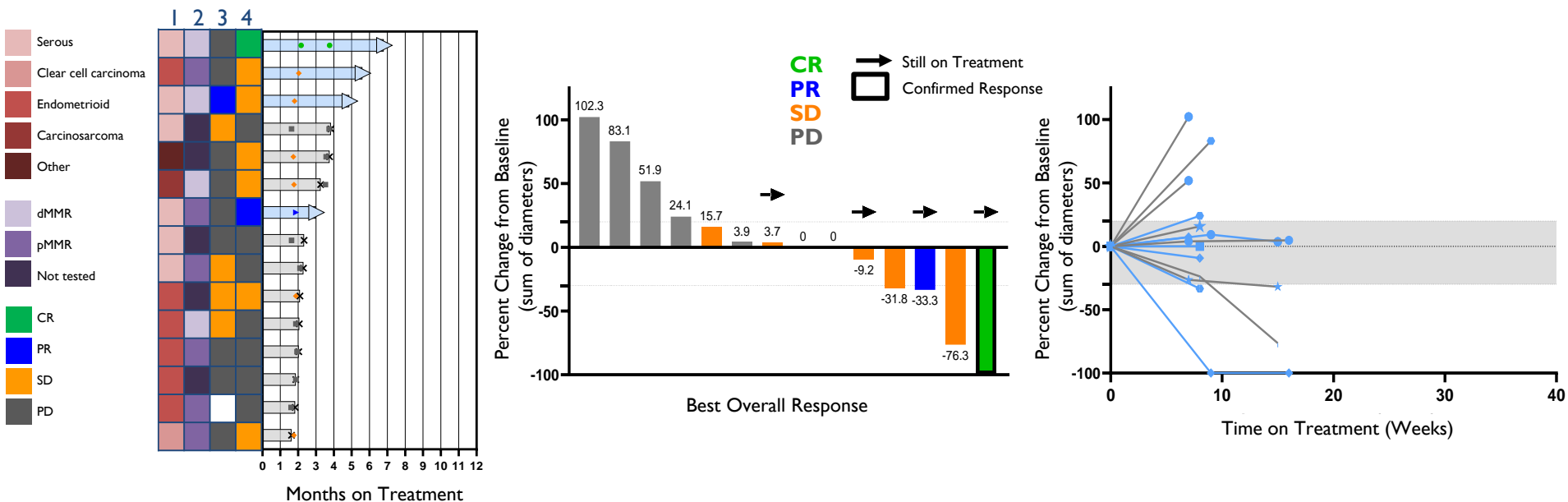
BOR = Best Overall Response, UNK = unknown, NA = not applicable, NT = not tested
 Data shown current as of 25Jul2024 and includes all efficacy-evaluable (at least one scan on-treatment) BM+ subjects

DEEP, RAPID RESPONSES SEEN IN PATIENTS WITH LARGE TUMOR LESIONS



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

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



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

Data current as of 25 July 2024, includes all BM- subjects enrolled at RP2D for LDG (10 mg/m²).
 1 – Histology; 2 – MMR; 3 – BOR on most recent prior line; 4 – BOR on ACR-368 + LDG

ENCOURAGING SAFETY PROFILE IN ENDOMETRIAL SUBJECTS

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

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

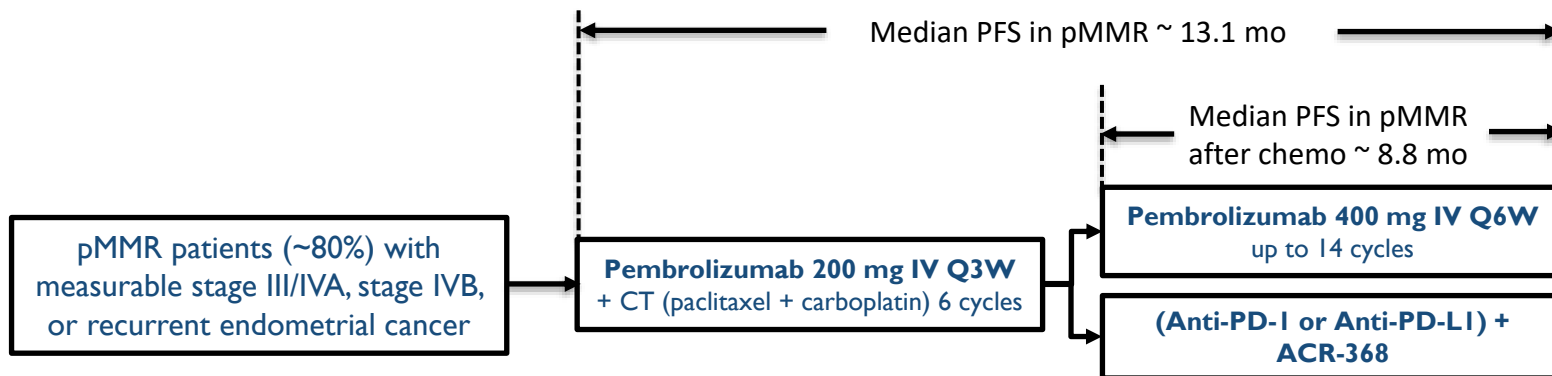
ACR-368 data current as of 25 July 2024 and includes the safety population of endometrial carcinoma subjects (any subject who has received at least one dose of ACR-368) enrolled (BM+ and BM-) and at the RP2D for LDG (BM-). Prophylactic G-CSF encouraged in BM+ and mandated in BM- subjects (compatible with q14d dosing regimen).

DEVELOPMENT PATH FOR ACR-368 IN ENDOMETRIAL CANCER

- Accelerated approval pathway
 - Ongoing single arm registrational intent Phase 2 monotherapy endometrial cancer trial represents the first potential approval opportunity for ACR-368
- Confirmatory trial strategy
 - Evaluating options to potentially move towards new front line setting
 - Randomization anti-PD-I vs [anti-PD-I/anti-PD-L1 + ACR-368] post [C/P + anti-PD-I] (sub-group analysis; MMR status in all-comer)*
 - Potential ≥ 2 nd line options:
 - ACR-368 + ULDG in all-comer patients

*Based on current clinical data showing cPRs in patients progressing on prior anti-PD-I, clinical safety data on ACR-368 + anti-PD-I, and strong rationale and preclinical data demonstrating additive/synergistic activity of ACR-368 and anti-PD-I (Refs: Do KT et al, Cancer Immunol Immunother, 2021; Lyer et al, Cancer Disc 2021; McGrail et al, Sci Transl Med 2021; Sen et al, Cancer Disc 2019)

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



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

- OncoSignature+ patients: $\sim(30,000 \text{ EC} \times 80\% \text{ pMMR} \times 30\% \text{ BM+} \times >10 \text{ months mPFS})$
- All-comer patients: $\sim(30,000 \text{ EC} \times 80\% \text{ pMMR} \times >10 \text{ months mPFS})$

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

- Enrollment is continuing in our ongoing multicenter phase 2 trials in ovarian and bladder cancer with planned update at a future date
- ACR-368 has also shown promising clinical activity in HPV+ squamous cell cancers (SCC), and sarcomas*
- HPV+ SCC are of increasing incidence (~50,000-60,000 new cases per year in the US) and includes ~70-80% of oropharyngeal H&N, ~20% of esophageal, ~90% of cervical, and 95% of anal cancers**
- SCCHN: Dr. C Chung, MD, Chair, Moffitt Cancer Center has begun an investigator-initiated trial with ACR-368 + ULDG in both HPV+ and HPV- SCCHN post anti-PD-1. IND cleared and site is activated
- **HPV+ SCC represent tumor types of high unmet need and attractive option for next Acrivon-sponsored trial(s) with ACR-368**

RECRUITING ⓘ

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

ClinicalTrials.gov ID ⓘ NCT06597565

Sponsor ⓘ H. Lee Moffitt Cancer Center and Research Institute

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

Last Update Posted ⓘ 2024-09-19

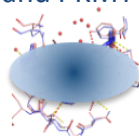
*Hong et al, CCR 2018, Slotkin et al, ASCO Annual Meeting 2022

**CDC 2023; ICO/IARC Information Centre on HPV and Cancer 2023; Gribb et al, Dela J Public Health 2023, NCI 2023

INTERNAL PIPELINE: AP3-BASED DRUG DISCOVERY

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

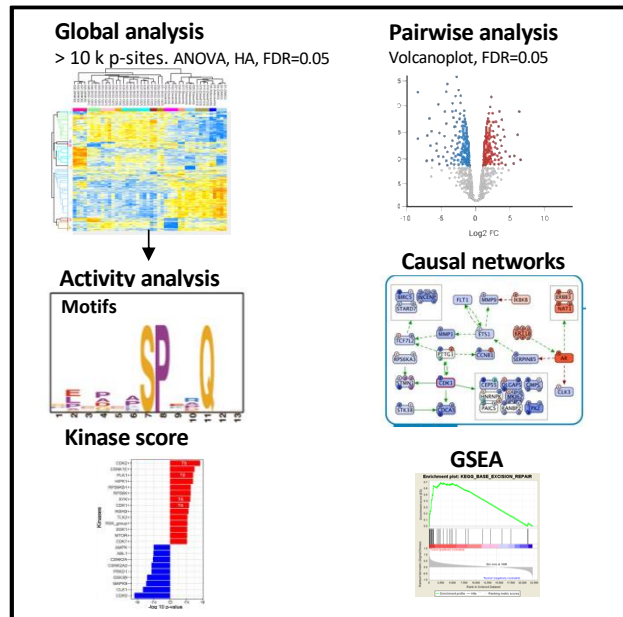
- >40 high resolution co-crystals (1.5-3.1 Å) and novel WEE1- and PKMYT1-selective structural series and lead candidates
- ACR-2316 a novel, potent, selective dual inhibitor
- Designed by AP3 to overcome WEE1 and PKMYT1 single inhibitor resistance
- IND cleared and clinical sites activated Q3 2024
- First in human dosing started October 2024



Program 2: Cell cycle inhibitor with an undisclosed target

- Anticipated development candidate 2025

High throughput AP3 profiling

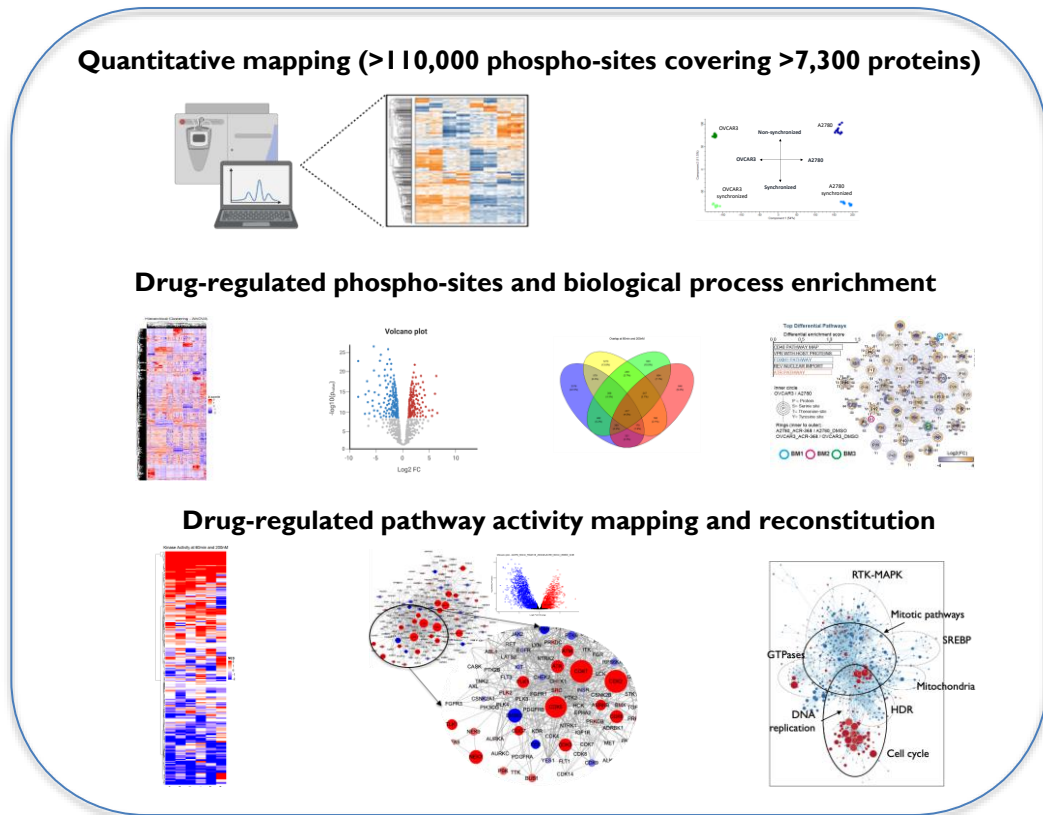
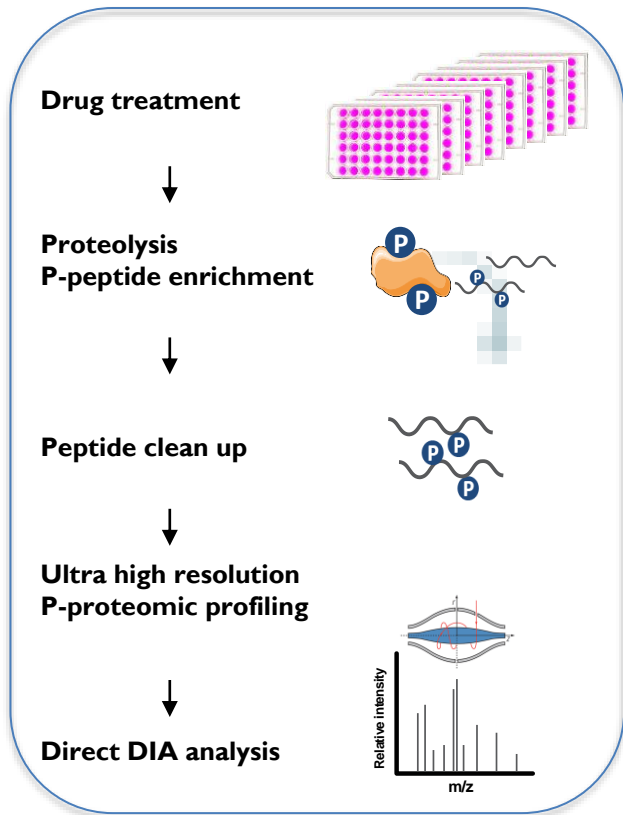


AP3 used for biologically relevant selectivity profiling

PROGRAM 1: ACR-2316, A NOVEL WEE1/PKMYTI INHIBITOR UNIQUELY ENABLED BY AP3

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

AP3: MACHINE LEARNING-DRIVEN STREAMLINED WORKFLOW FOR RATIONAL DRUG DESIGN AND BIOLOGICAL SAR



Week 0

Turn-around
<2 weeks

Week2

High resolution and throughput MS-based P-proteomics

Proprietary pipe for automated AP3 analyses with actionable results

AP3: TIGHT, HIGH-RESOLUTION DATA WITH DEEP COVERAGE

117,200 p-sites

43,000 p-sites

QC MS Data

Data Clean Up

QC Processed Data

Volcano Plots

Hierarchical Clustering

Consensus Sequence Motif

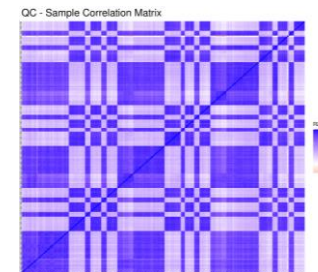
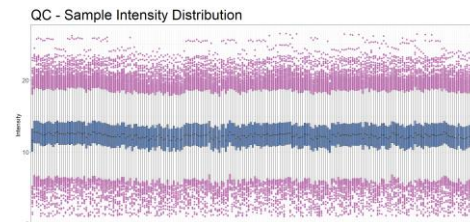
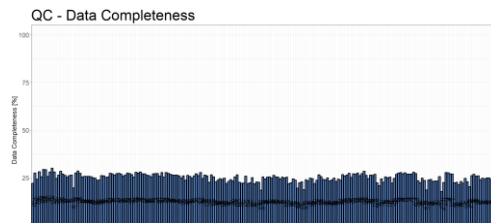
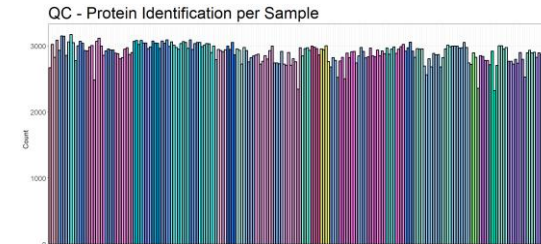
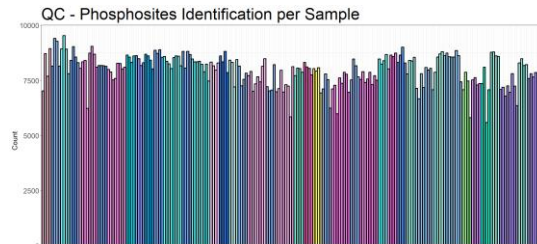
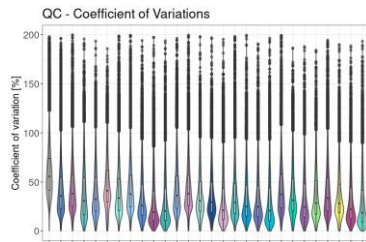
Kinase Inference

Pathway Enrichment

Functional Annotation

Network Mapping

Biomarkers

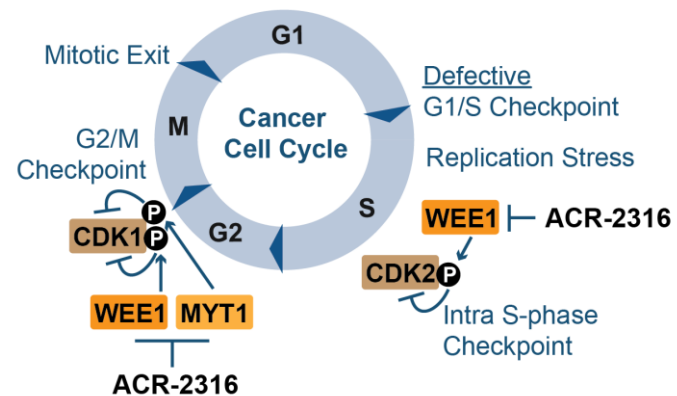


- ✓ Acrivon proprietary compound data (>100 million data points per experiment)
- ✓ Several hundred samples (quadruplicates) in each experiment; >100 compounds profiled
- ✓ Miniaturized, high throughput, scalable: <2 week turn-around, automated AI computational analyses in 1 day

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

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

- WEE1 and PKMYT1 regulate S and G2-M cell cycle checkpoints to ensure proper DNA replication and mitotic completion
- Defective DNA repair is highly prevalent in cancers, creating a dependency on checkpoint proteins
- WEE1 inhibition propagates genomic instability by premature DNA replication and cell cycle progression
- PKMYT1 inhibition results in premature mitotic entry



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

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

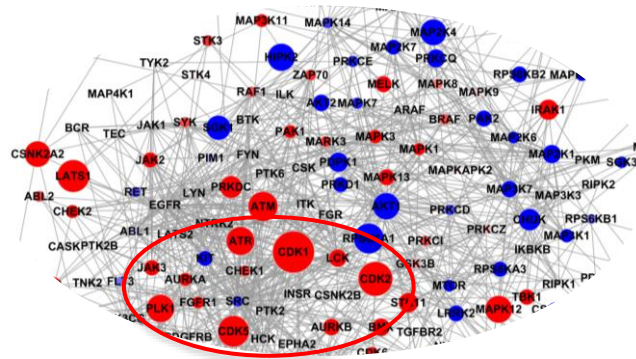
Program goals (superior therapeutic index):

- **Superior single agent activity (AP3)**
 - Potent activation of CDK1, CDK2, and PLK1 and quenching of resistance through balanced WEE1/PKMYT1 inhibition to ensure robust pro-apoptotic tumor death
- **High selectivity for minimal AEs (co-crystallography)**
 - Structure-guided design to limit adverse events (AEs) to be strictly mechanism-based, transient, short-lived
- **Streamlined clinical development (ACR-2316 OncoSignature)**
 - To identify/prioritize sensitive indications prior to clinical start and for drug target engagement-based dose optimization during Phase I

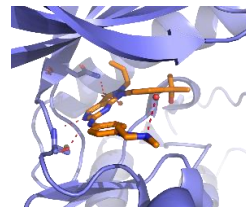
ACR-2316: Rationally designed WEE1/PKMYT1 inhibitor

- ✓ Superior anti-tumor efficacy with complete tumor regression across models
- ✓ High selectivity ensures transient, short-lived, mild AEs
- ✓ Potent WEE1 inhibition, balanced PKMYT1 inhibition, overcomes resistance and enables robust activation of CDK1, CDK2, and PLK1 for mitotic catastrophe

AP3 used for pathway-based optimization to achieve superior single agent activity



Co-crystallography for drug design and selectivity



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

ACR-2316 SHOWS SUPERIOR PRECLINICAL POTENCY VS BENCHMARK WEE1/PKMYT1 INHIBITORS¹

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

Black text = Acrivon Data; Grey text = Schrodinger Data

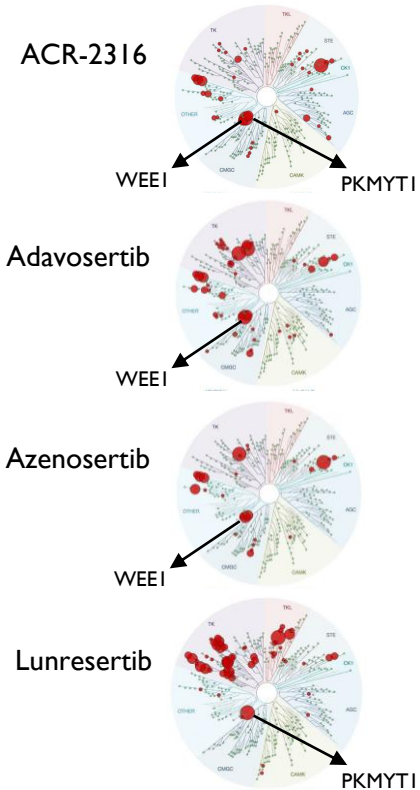
¹Head-to-head preclinical studies against benchmarks with clinical data

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

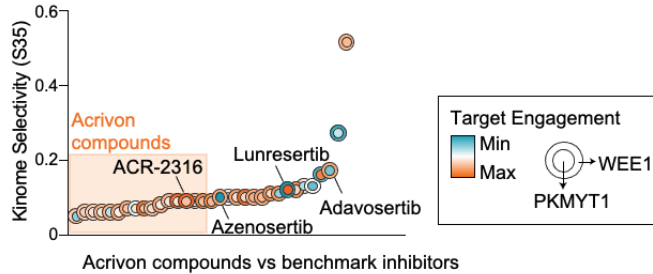
³SGR-3515 preclinical data presented at ENA-2024

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

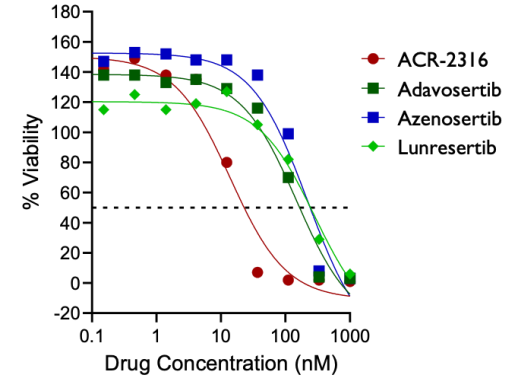
KinomeScan (468 kinases @ 1 μ M)



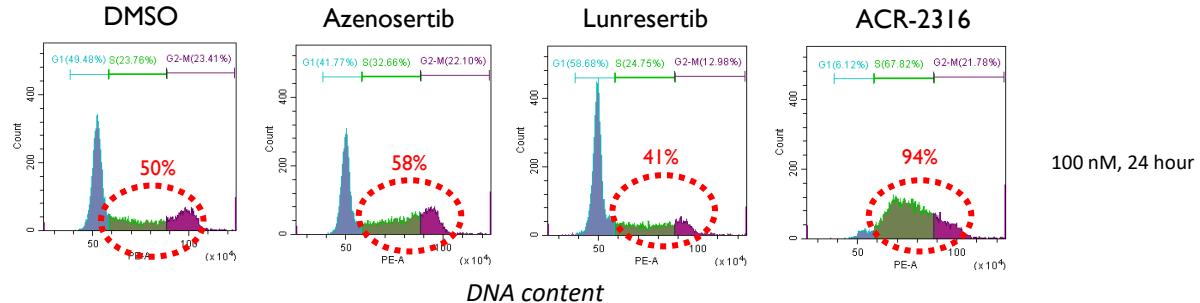
ACR-2316 is highly selective (KinomeScan)



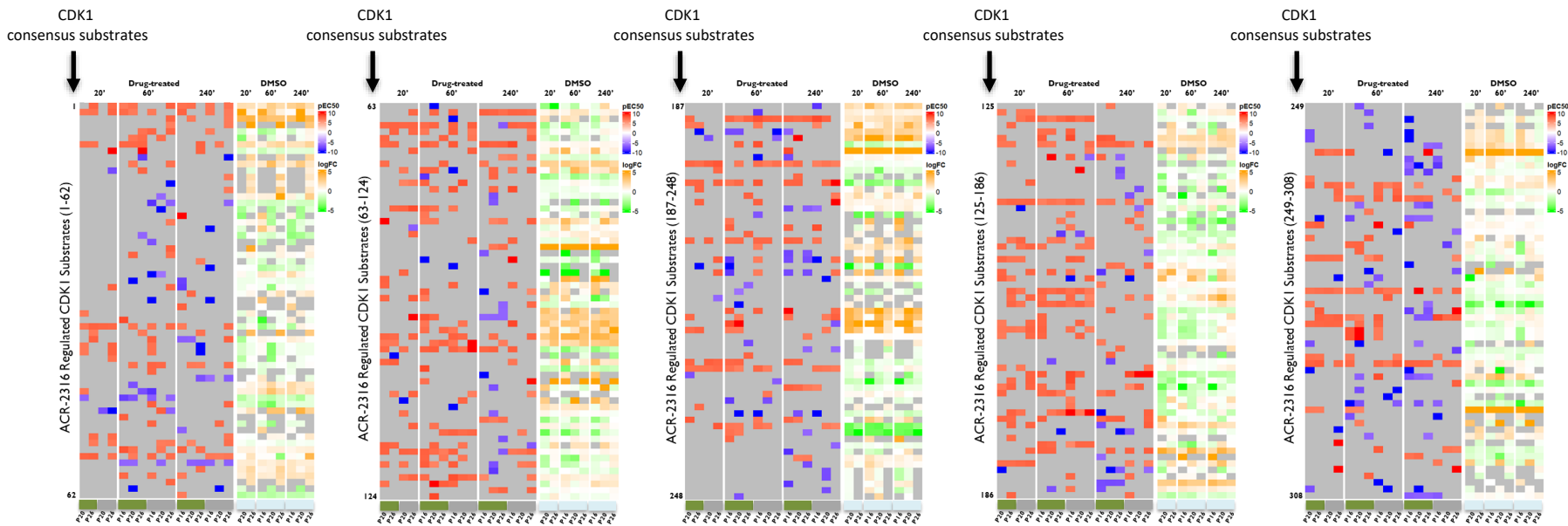
ACR-2316 potently inhibits cancer cell viability



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

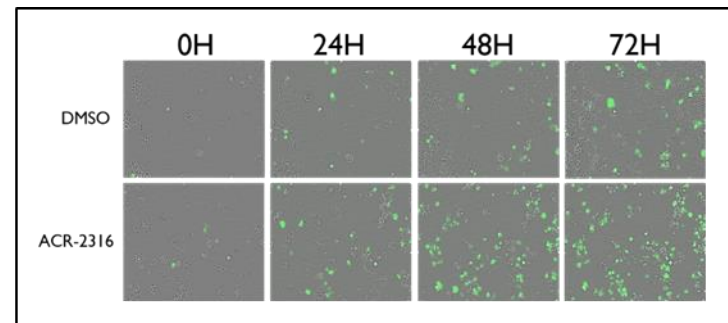
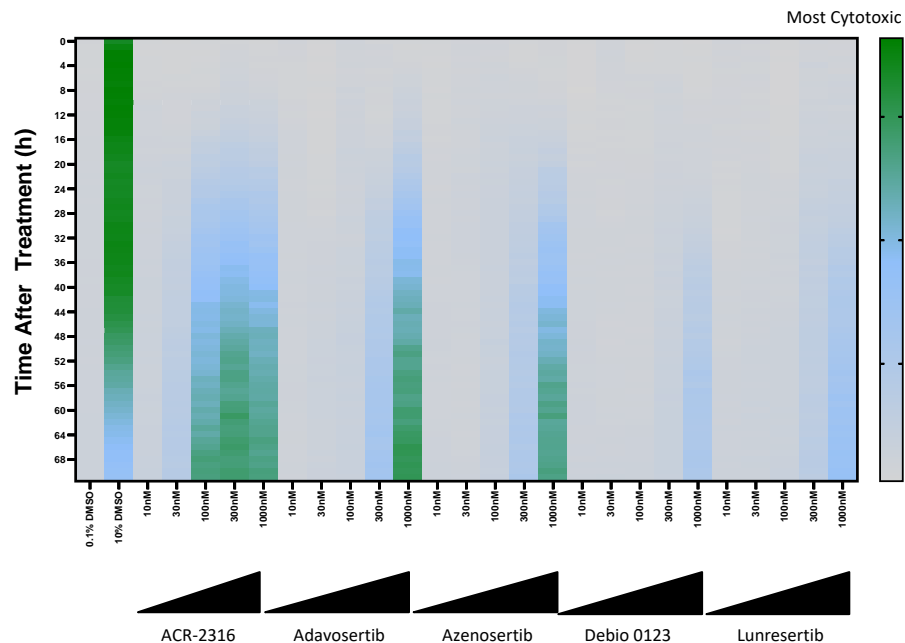


ACR-2316 RESULTS IN STRONG ACTIVATION OF CDK1 ACROSS CELL LINES



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

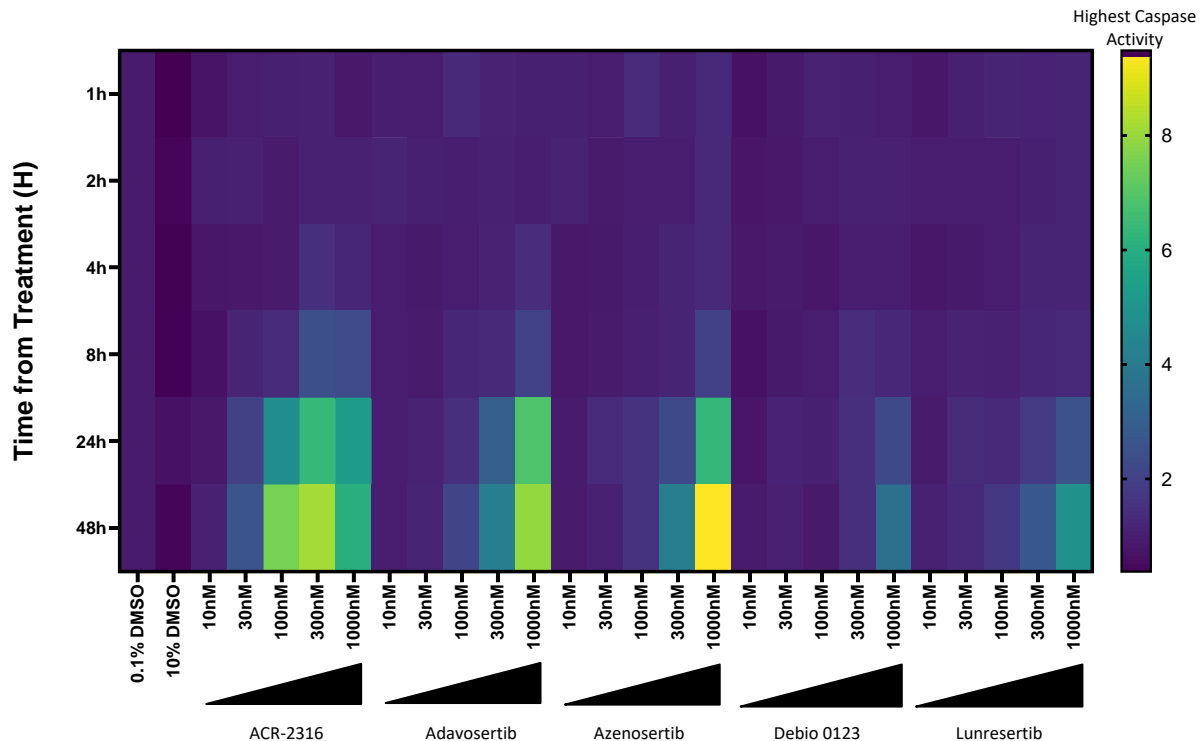
ACR-2316 INDUCES POTENT CELL DEATH COMPARED TO BENCHMARK WEE1 AND PKMYTI INHIBITORS



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

CellTox-Green Assay

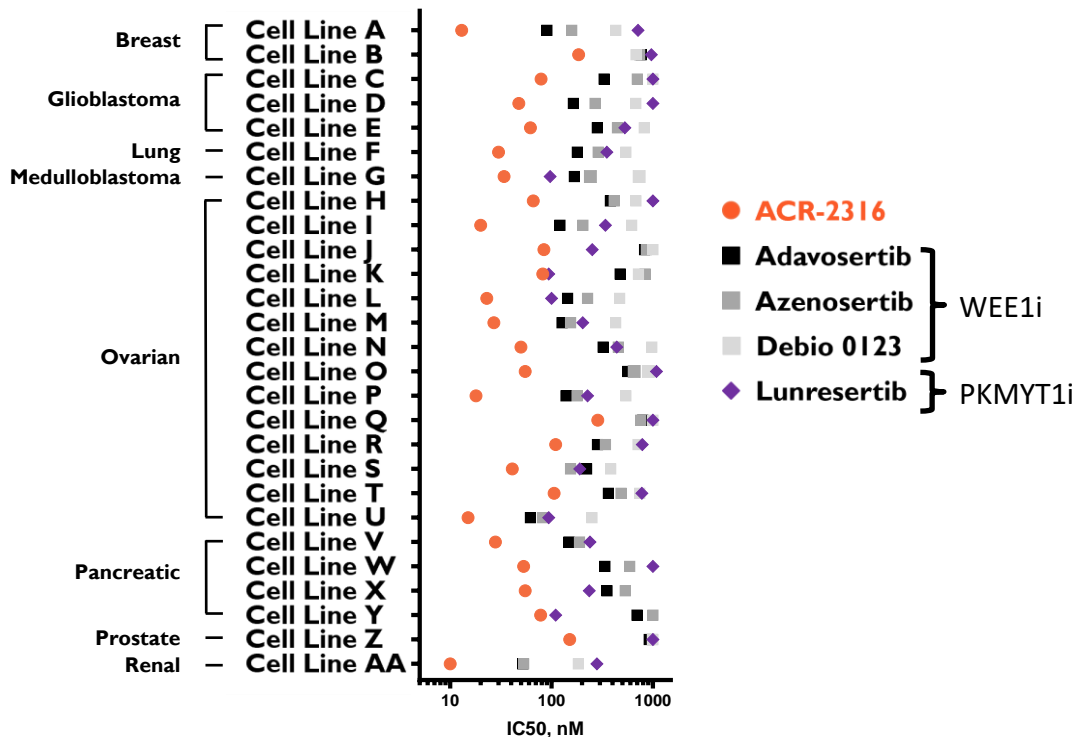
ACR-2316 INDUCES POTENT CASPASE 3/7 CLEAVAGE COMPARED TO BENCHMARK WEE1 OR PKMYTI INHIBITORS



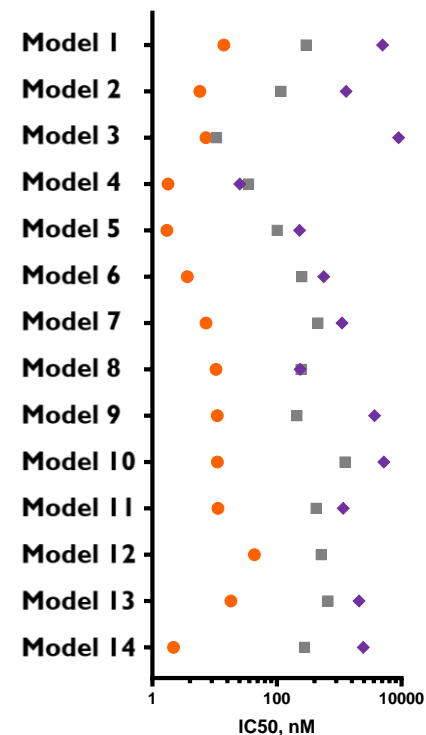
Caspase 3/7-Glo Assay

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

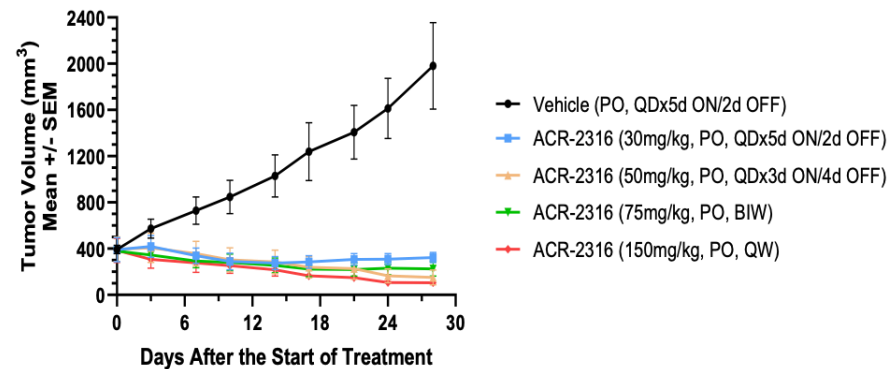
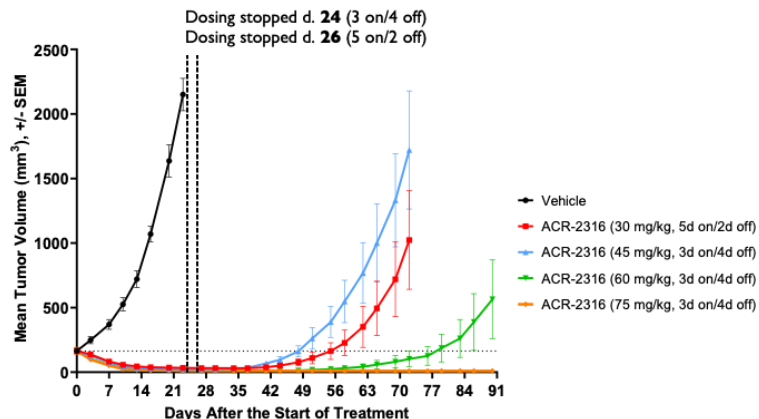
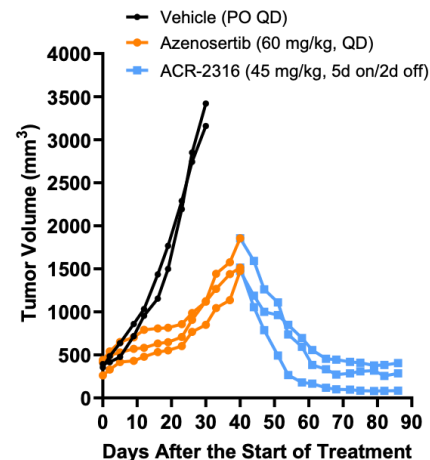
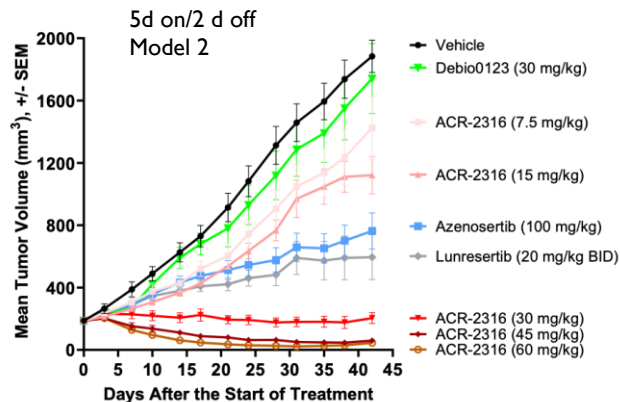
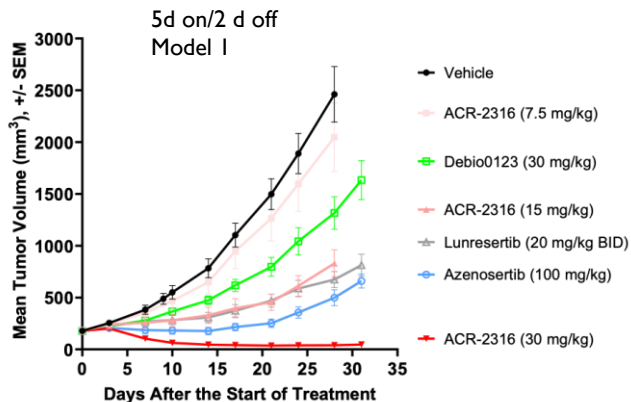
Human tumor cell lines (not genetically selected)



Patient-derived *ex vivo* ovarian tumor models



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



ACR-2316 - FAVORABLE PRECLINICAL SAFETY PROFILE

Mice:

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

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

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

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

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

Program Goals

- 1 Superior single agent activity
- 2 High selectivity and potency
- 3 Favorable safety profile
- 4 Streamlined clinical development

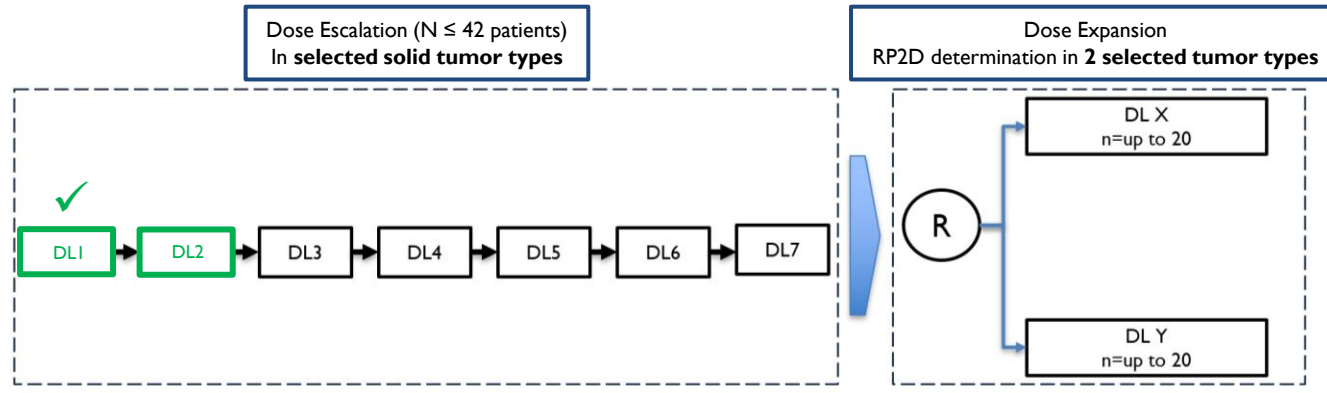
AP3-Enabled SAR

Demonstrated Preclinical Results

- Superior* single agent anti-tumor activity through robust CDK1, CDK2, and PLK1 activation and elimination of dominant resistance mechanisms through balanced WEE1 and PKMYT1 inhibition
- 5-20-fold more potent* in preclinical models than clinical benchmarks
- High selectivity results in adverse events limited to transient, short-lived, mechanism-based, reversible
- Broad preclinical therapeutic index and anti-tumor activity across dosing regimens
- AP3-based identification of PD biomarkers and prioritization of promising indications

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

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

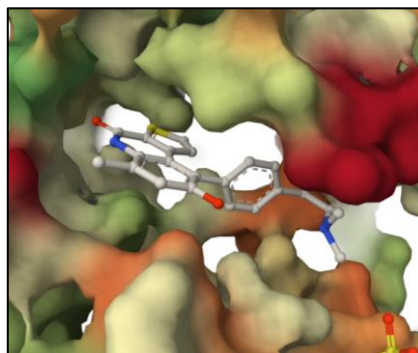
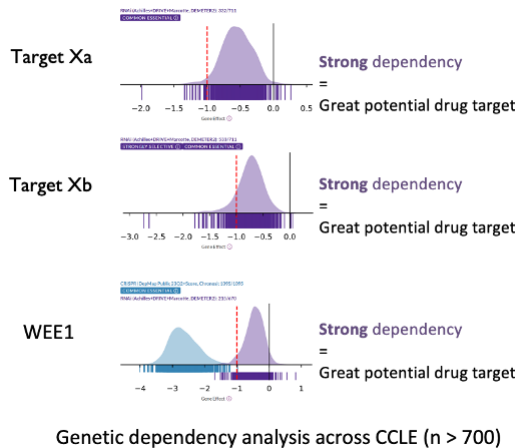


Aiming for streamlined clinical development:

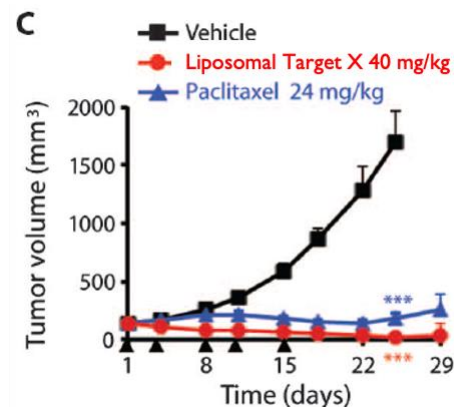
- ACR-2316 advanced in 15 months from initial lead into Phase I uniquely enabled by AP3
- AP3-based indication finding has identified highly commercially attractive indications
- Dose optimization guided by drug target engagement aligned with Project Optimus

PROGRAM 2: CELL CYCLE REGULATOR (UNDISCLOSED TARGET)

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



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



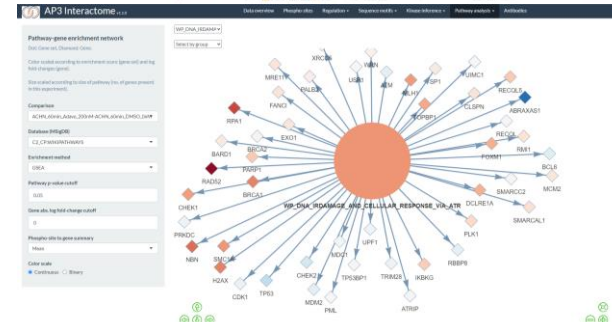
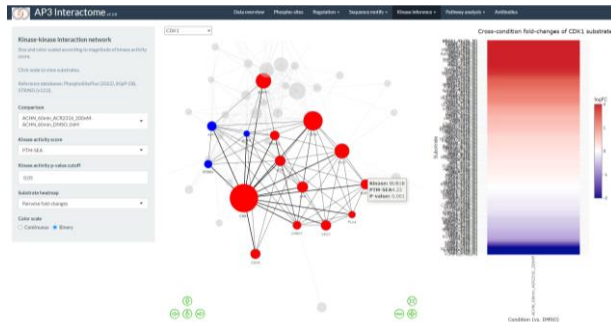
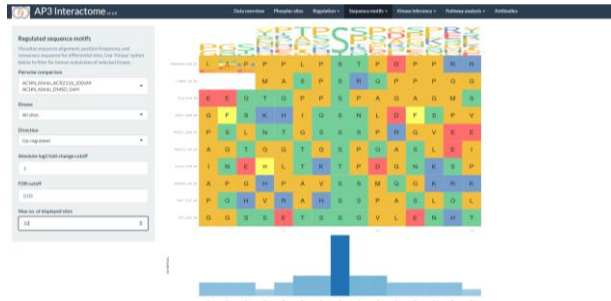
Development candidate 2025

AP3 INTERACTOME V.2: PROPRIETARY INTERACTIVE DATA ANALYSIS INFRASTRUCTURE

Actionable data across all AP3 experiments accessible for all Acvion scientists
Fully scripted, algorithm-based machine learning-enabled pathway and biomarker analyses

~150,000 phosphosites

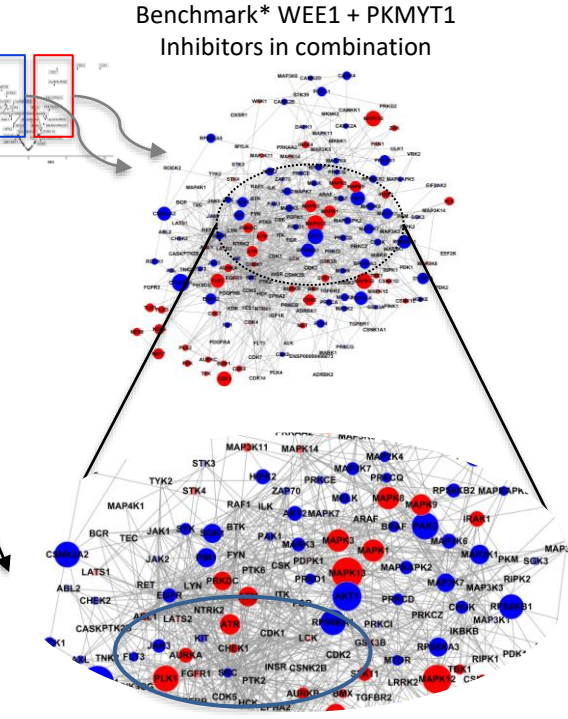
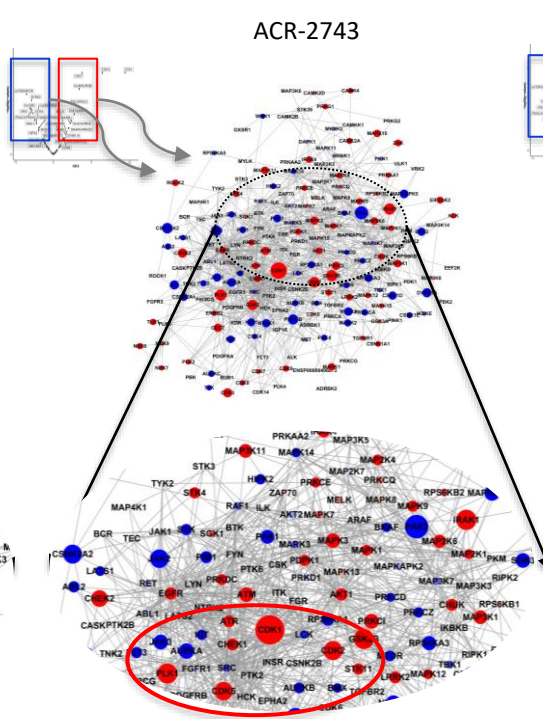
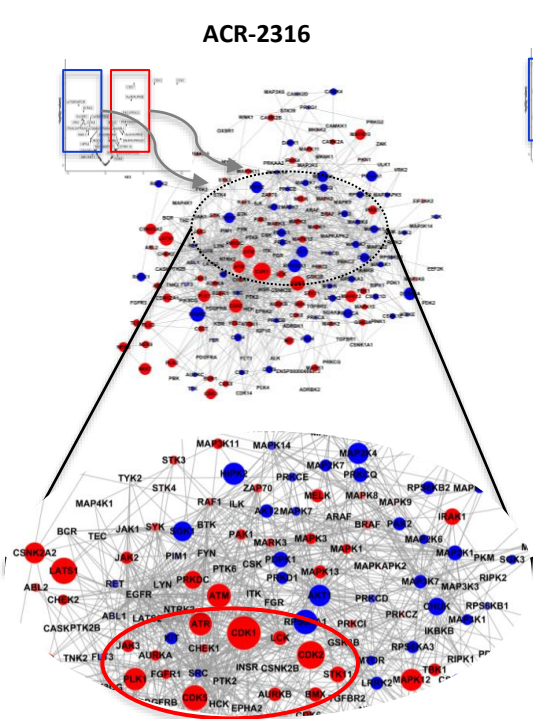
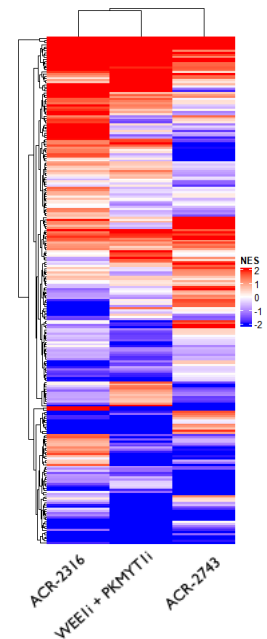
~50,000 phosphosites



OPTIMIZED DUAL INHIBITORS SHOW DESIRABLE PATHWAY EFFECTS

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

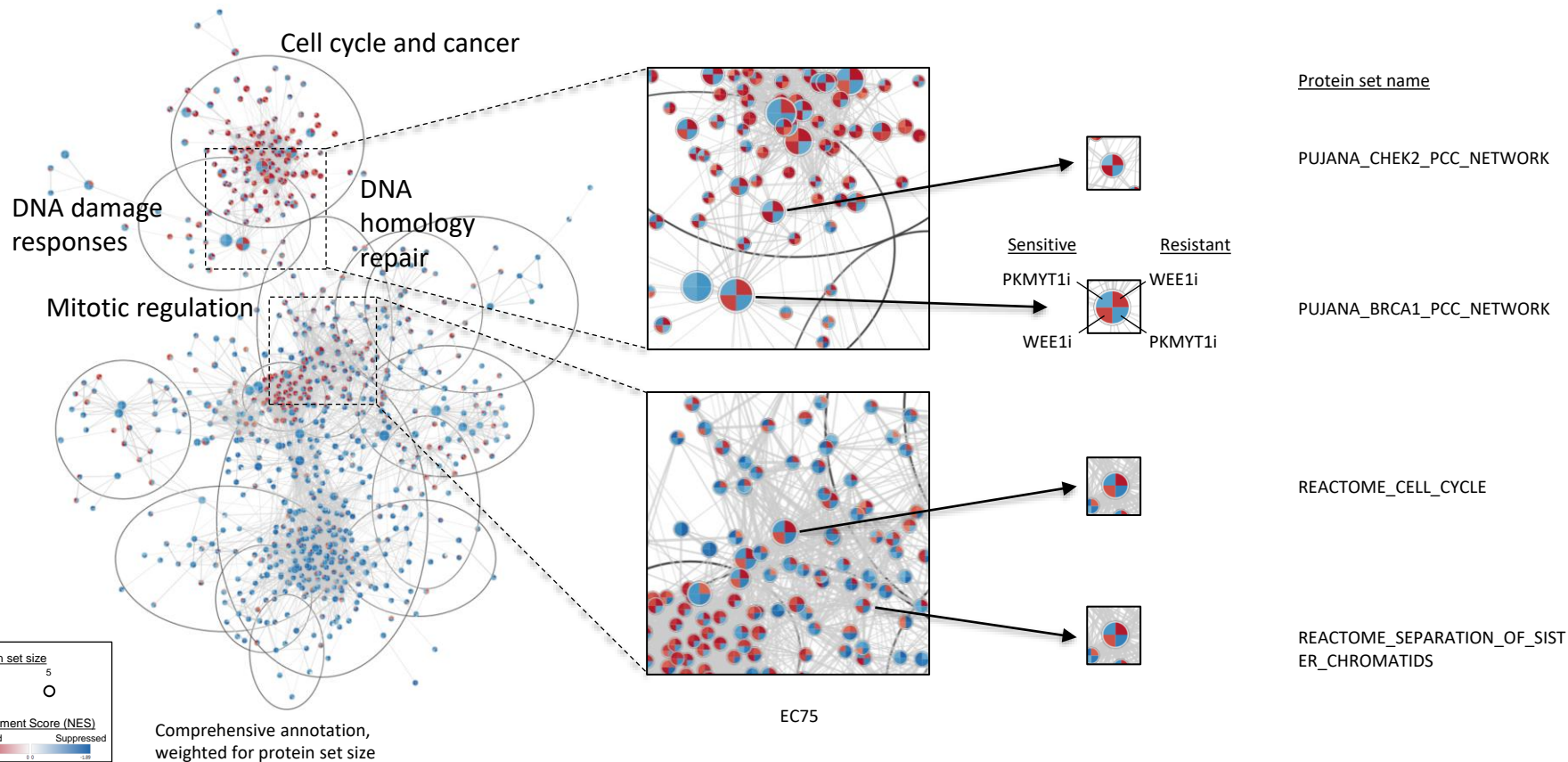
Substrate motif-inferred kinase activities



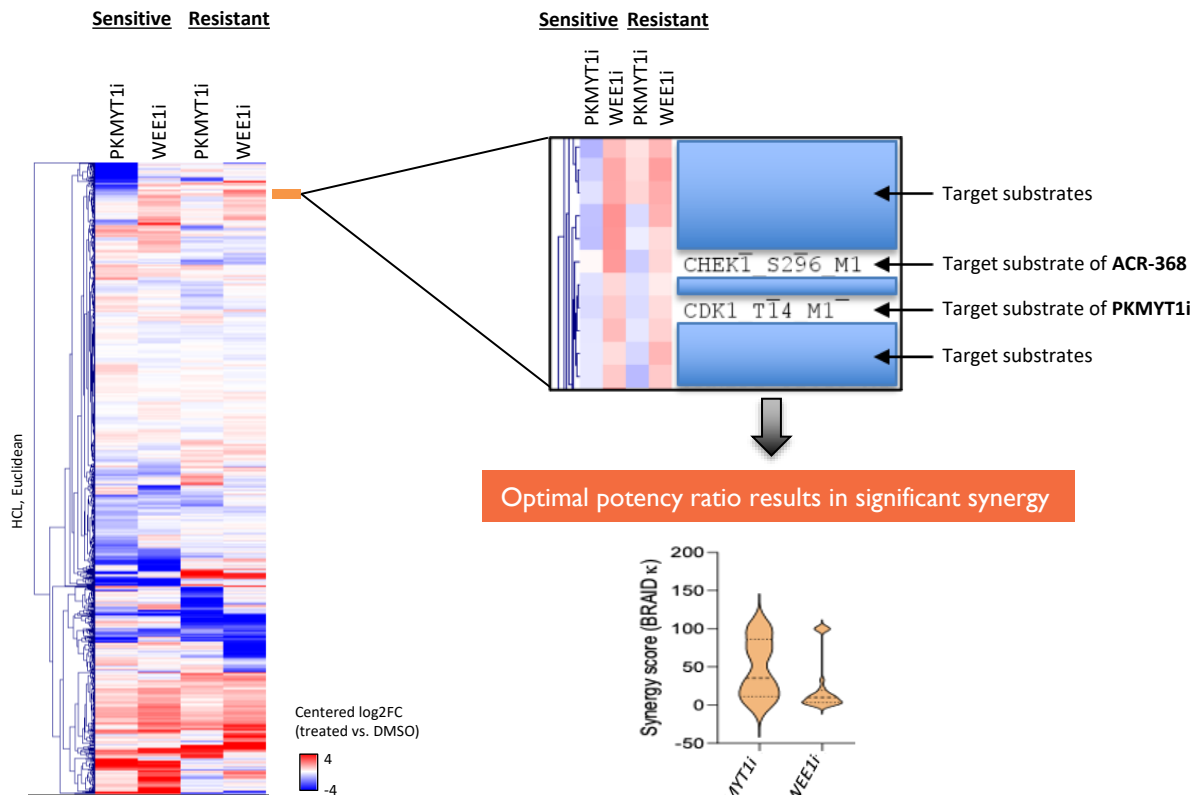
Kinase activity based on proprietary PTM-SEA-based hybrid workflow and analyses

*Clinical-stage selective WEE1 and PKMYT1 inhibitors

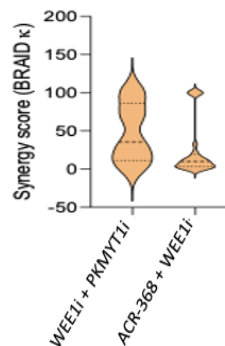
AP3-DERIVED DUAL POTENCY OPTIMIZATION TO OVERCOME WEE1 INHIBITOR RESISTANCE: RECIPROCAL QUENCHING



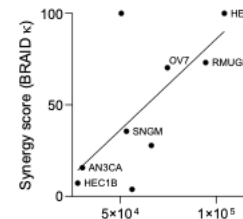
AP3 RECIPROCAL QUENCHING REVEALS OPTIMAL TARGET POTENCY PROFILE FOR DUAL WEE1/PKMYT1 INHIBITOR



Optimal potency ratio results in significant synergy



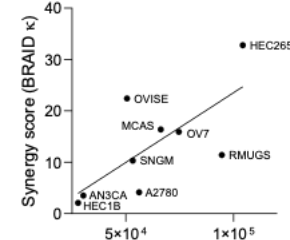
WEE1i and PKMYT1i dual inhibition synergy



WEE1 inhibitor sensitivity (Mean AUC)

Pearson $r = 0.68$
p value = 0.0459

WEE1i and ACR-368

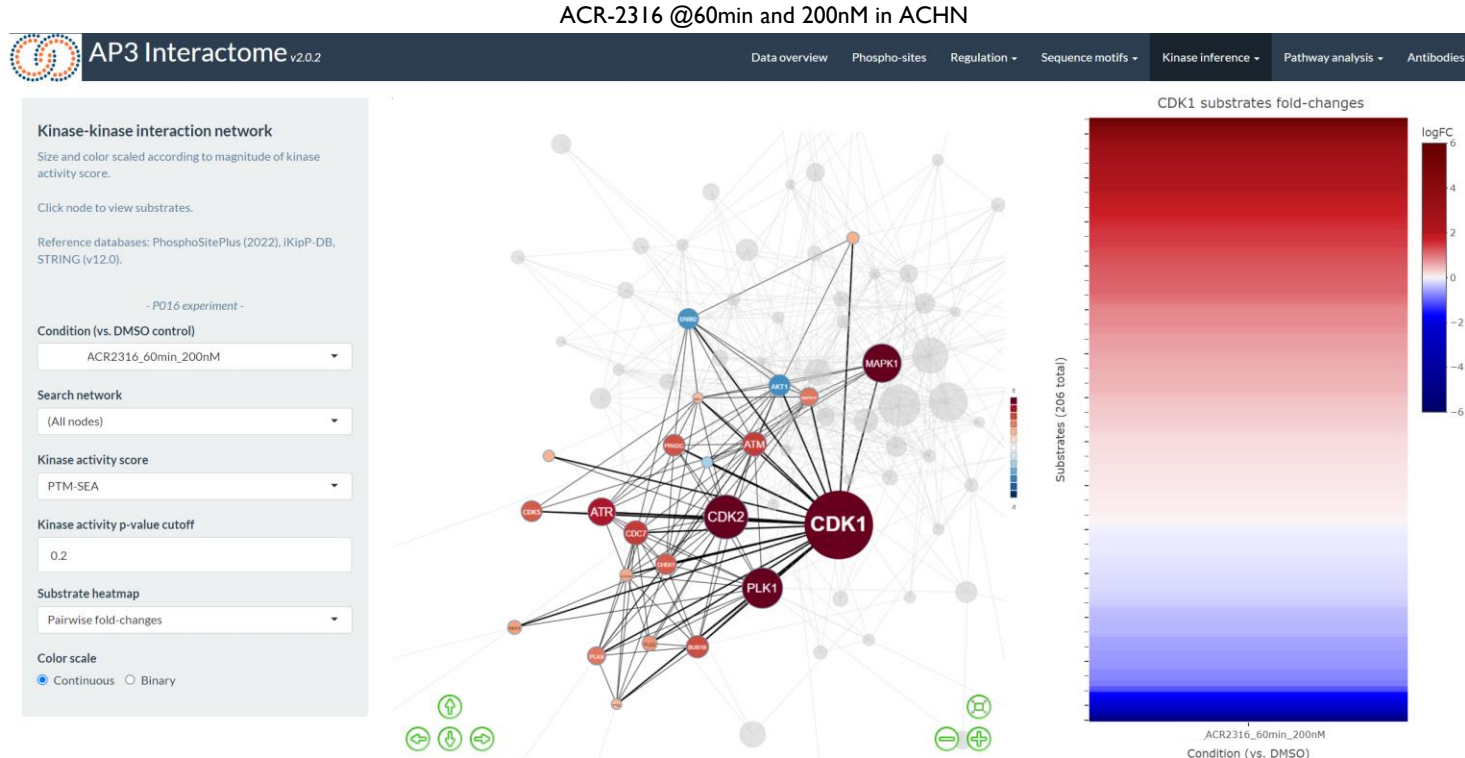


WEE1 inhibitor sensitivity (Mean AUC)

Pearson $r = 0.71$
p value = 0.0324

ACR-2316 INDUCES POTENT ACTIVATION OF PRO-APOPTOTIC MITOTIC KINASES IN SENSITIVE TUMOR CELLS

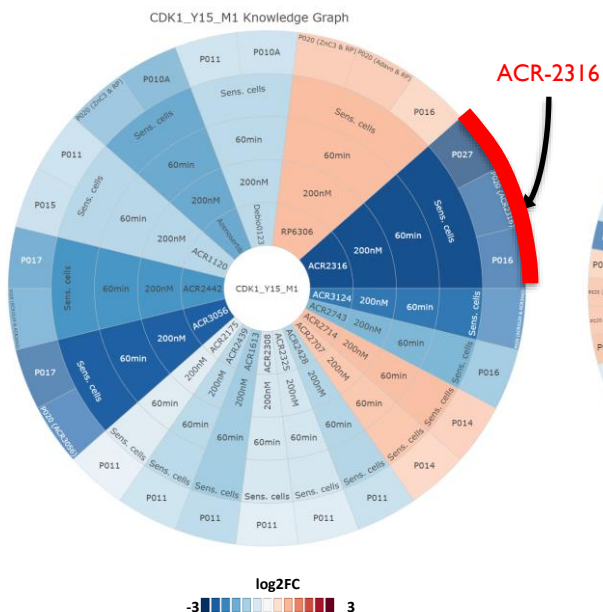
- Robust activation of CDK1 with ACR-2316 exemplified by enrichment of 206 upregulated substrates of CDK1



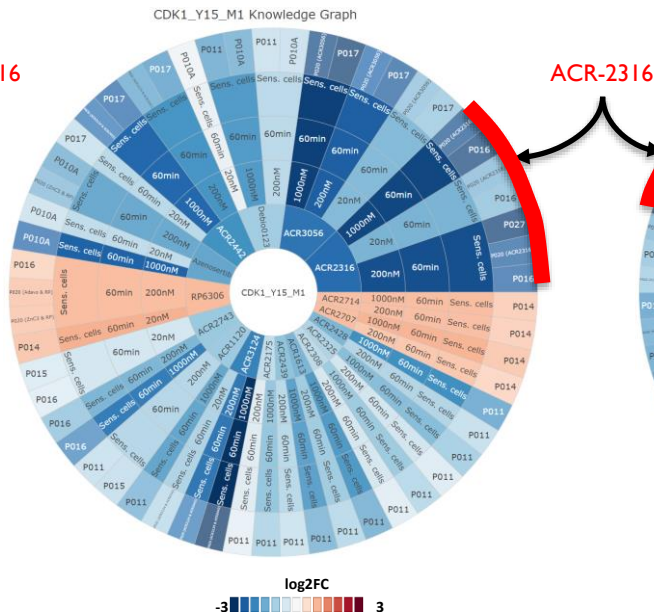
ROBUST POTENT INHIBITION OF CDKI CONSENSUS SUBSTRATE Y15 BY ACR-2316

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

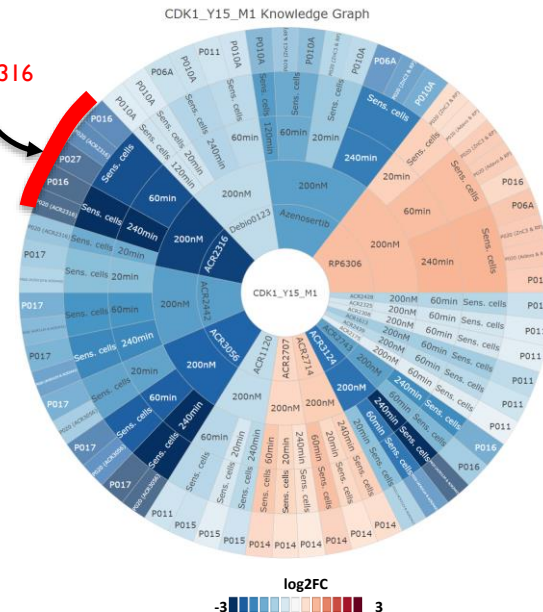
Comparison
@60min and 200nM in ACHN



Dose-dependent comparison
@ 60min in ACHN



Time-dependent comparison
@ 200nM in ACHN



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

Home

ACR2316
Profiled in 12 experiments.

Features
Kinases

No. of top features
10

Filter fully-imputed sites

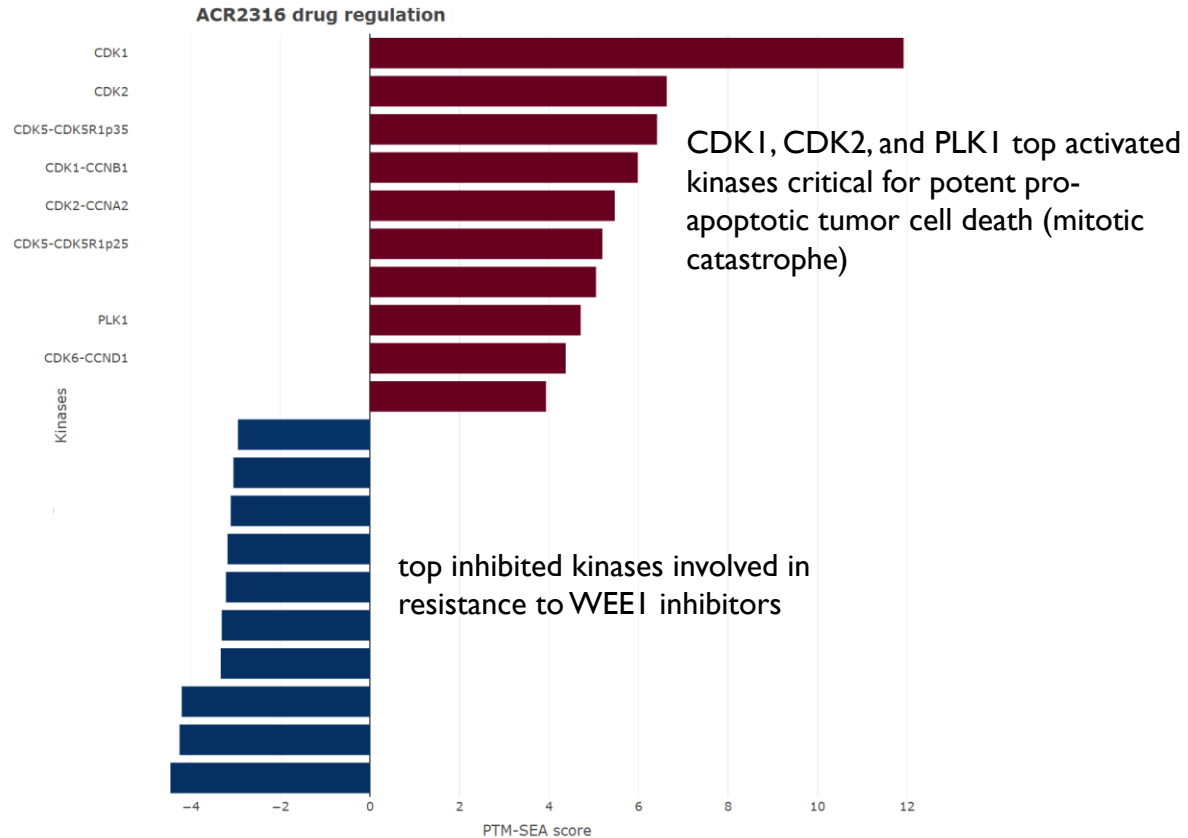
Antibody-available only (sites)

Dosage
200nM

Timepoint
60min

Cell line

Export



DATA DRIVEN EXECUTION AND VALUE CREATION

Recent Accomplishments (Last 12 Months)

- ✓ Positive ACR-368 data (ESMO 2024) in registrational intent endometrial cancer trial (ORR >60%; OncoSignature validation $p = 0.009$)
- ✓ Positive initial ACR-368 clinical data in ovarian and endometrial cancer patients (ORR = 50%) in Q2 2024
- ✓ IND clearance for ACR-2316 (Q3 2024) and first patient dosed in Q4 2024 (2Q ahead of schedule) with initial lead to Ph I initiation achieved in 15 months, uniquely enabled by AP3; second dosing cohort initiated
- ✓ Corporate R&D Events (Q2 and Q3 2024) presenting positive clinical and preclinical pipeline data and AI/ML-driven AP3 Interactome
- ✓ Presented preclinical data on ACR-2316 and ACR-368 resistance mechanisms uncovered by AP3 (AACR Q2 2024, ENA Q4 2024, HUPQ Q4 2024)
- ✓ Completed Phase 1b and initiated Phase 2 study of ACR-368 + LDG for OncoSignature-negative patients Q1 2024
- ✓ Granted Breakthrough Device Designation for ACR-368 OncoSignature Assay for Ovarian Cancer 4Q 2023
- ✓ Completed oversubscribed \$130M PIPE financing at premium Q2 2024

Anticipated Next Milestones

Phase 2 program updates for ACR-368 IH 2025

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

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

Target prioritization and indication finding to support novel programs in autoimmune/inflammatory/fibrotic diseases leveraging AI/ML-driven AP3 and integrated AP3 Interactome proprietary data set and analyses

FINANCIAL HIGHLIGHTS

Cash and marketable securities

\$202.8M

Balance sheet
30-Sept-2024

Projected runway into

H2'26

Current operating plan, assuming
no additional financing

Fully Diluted Shares Outstanding

43.7M

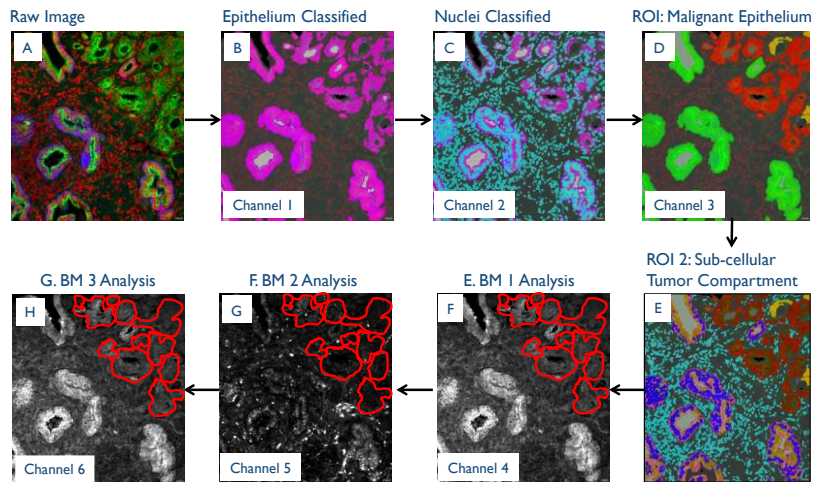
Including shares, pre-funded
warrants and equity grants
outstanding 30-Sept-2024

Note: Unaudited.



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 <i>in situ</i> 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

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

(2015)

Peter Blume-Jensen¹, David M. Berman², David L. Rimm³, Michail Shipitsin¹, Mathew Putzi⁴, Thomas P. Nifong¹, Clayton Small¹, Sibgat Choudhury¹, Teresa Capela¹, Louis Coupal⁵, Christina Ernst¹, Aeron Hurley¹, Alex Kaprelyants¹, Hua Chang¹, Eldar Giladi¹, Julie Nardone¹, James Dunyak¹, Massimo Loda⁶, Eric A. Klein⁷, Cristina Magi-Galluzzi⁸, Mathieu Latour⁹, Jonathan I. Epstein¹⁰, Philip Kantoff⁶, and Fred Saad⁹

- 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



Sci Transl Med
2: 1-14 (2010)

RESEARCH ARTICLE

CANCER DRUG DEVELOPMENT

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

Jannik N. Andersen,^{1*} Sriram Sathyanarayanan,^{1*} Alessandra Di Bacco,¹ An Chi,¹ Theresa Zhang,¹ Albert H. Chen,¹ Brian Dolinski,¹ Manfred Kraus,¹ Brian Roberts,¹ William Arthur,² Rich A. Klinghoffer,^{1†} Diana Gargano,^{1‡} Lixia Li,¹ Igor Feldman,¹ Bethany Lynch,¹ John Rush,³ Ronald C. Hendrickson,^{4§} Peter Blume-Jensen,^{1§||} Cloud P. Paweletz¹

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



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



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A discovery strategy for novel cancer biomarkers

OLSEN LAB-EXAMPLES OF DEEP PROTEOMICS DRUG PROFILING

Science Signaling (2018)

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

SCIENCE SIGNALING | RESEARCH RESOURCE

CANCER

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

Kristina B. Emdal^{1,2}, Anna Kathrine Pedersen^{1,2}, Doris B. Bekker-Jensen¹, Alicia Lundby^{1,3}, Shara Chawky¹, Kåthe De Preter⁴, Chiara Francavilla^{1,5,6}, Jesper V. Olsen^{1,6}

Cell Reports (2018)

SHP2-i: SHP099 -allosteric inhibitor.

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

Tawee S. Bath^{1,2}, Moreno Pagani^{1,2}, Anamaria Pfeiffer¹, Maxim A.X. Tollemans¹, Chiara Francavilla^{1,3,4}, and Jesper V. Olsen^{1,6}

¹Proteomics Program, Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Sciences, University of Copenhagen, Blegdamesvej 3B, 2200 Copenhagen, Denmark
²Cellular Stress Signaling Group, Department of Cellular and Molecular Research, Faculty of Health and Aging, University of Copenhagen, 2200 Copenhagen, Denmark
³School of Biological Sciences, FHM, University of Manchester, Oxford Road, Manchester M13 9PL, UK
⁴These authors contributed equally
⁵Lead Contact
⁶Correspondence: olsen@proteomicscenter.au.dk (J.V.O.), jesper.olsen@pro.ku.dk (J.V.O.)
<https://doi.org/10.1016/j.celrep.2018.02.028>

Cell Reports (2017)

CHK1-i: SCH900776, ATM-i: KU55933

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

Stephanie Munk^{1,2,3}, Jin Ohi Saperstein^{1,2}, Zhewen Xia^{1,2}, Tamara Singh Bath¹, Giulia Franciosa¹, Louise von Stechow¹, Andres Jaegerin Lopez-Contreras¹, Alfred Cornelis Ots Vertgaal^{1,2,3}, and Jesper Velgaard Olsen^{1,4,5,6}
¹Proteomics Program, Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Sciences, University of Copenhagen, 2200 Copenhagen, Denmark
²Center for Chromosome Stability and Center for Health Aging, Institute for Cellular and Molecular Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, 2200 Copenhagen, Denmark
³Department of Molecular Cell Biology, Leiden University Medical Center, 2300 RC Leiden, the Netherlands
⁴These authors contributed equally
⁵Lead Contact
⁶Correspondence: ohi@proteomicscenter.au.dk (J.V.O.), jesper.olsen@pro.ku.dk (J.V.O.)
<https://doi.org/10.1016/j.celrep.2017.09.058>

Cell Reports (2017)

CDK7-i: THZ-1
Phosphoproteomics of Primary Cells Reveals Druggable Kinase Signatures in Ovarian Cancer

Chiara Francavilla^{1,2,3}, Michela Lupia^{1,2}, Kalligki Tsibou^{1,2,3}, Alessandro Villa^{1,2,3}, Katarzyna Kowalczyk^{1,2}, Rina Rakwiewicze-Janus-Christiansen¹, Giovanni Bertini¹, Stefano Costantini¹, Sven Brannk¹, Lars J. Jensen¹, Ugo Covellari^{1,2}, and Jesper V. Olsen^{1,2,3,4}
¹Proteomics Program, Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Sciences, University of Copenhagen, Blegdamesvej 3B, 2200 Copenhagen, Denmark
²Unit of Cytopathological Oncology Research, Program of Cytopathological Oncology, European Institute of Oncology, Via Risparmio 485, 20143 Milan, Italy
³Research Systems Biology Program, Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Sciences, University of Copenhagen, Blegdamesvej 3B, 2200 Copenhagen, Denmark
⁴Program of Molecular Medicine, European Institute of Oncology, Via Risparmio 485, 20143 Milan, Italy
⁵Division of Molecular and Cellular Functions, School of Biological Sciences, Faculty of Biology, Medicine and Health, the University of Manchester, Manchester M13 9PL, UK
⁶Co-lead author
⁷Present address: Division of Molecular and Cellular Functions, School of Biological Sciences, Faculty of Biology, Medicine and Health, the University of Manchester, Manchester M13 9PL, UK
⁸Present address: Department of Oncology, Lombard Comprehensive Cancer Center, Georgetown University, Washington, DC 20057, USA
⁹Present address: Pflücker AG, Chiemgau, Deutschland
¹⁰Lead Contact
¹¹Correspondence: chiara.francavilla@proteomicscenter.au.dk (J.V.O.), ugo.covellari@pro.ku.dk (J.V.O.)
<https://doi.org/10.1016/j.celrep.2017.03.075>

Cell Systems (2017)

Deepest proteome resolution of a human cell to date

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

Doris B. Bekker-Jensen¹, Christian D. Kelstrup^{1,2}, Tamara S. Bath¹, Sara C. Larsen¹, Christa Hedrup¹, Jesper B. Bransum¹, Karina D. Sørensen¹, Soren Hoyer¹, Torben F. Omkar¹, Claus L. Andersen¹, Michael L. Nielsen¹, and Jesper V. Olsen^{1,2}
¹Proteomics Program, Novo Nordisk Foundation Center for Protein Research, University of Copenhagen, Blegdamesvej 3B, 2200 Copenhagen, Denmark
²Department of Molecular Medicine and Clinical Medicine, Aarhus University Hospital, Aarhus University, Palle Juul-Jensens Boulevard 99, 8200 Aarhus, Denmark
³Institute of Pathology, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus, Denmark
⁴These authors contributed equally
⁵Lead Contact
⁶Correspondence: christian.kelstrup@pro.ku.dk (C.D.K.), jesper.olsen@pro.ku.dk (J.V.O.)
<http://dx.doi.org/10.1016/j.celsys.2017.05.009>

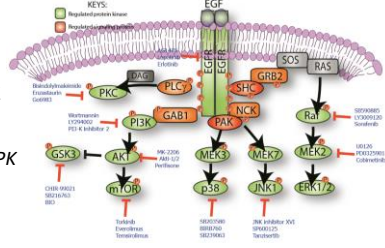
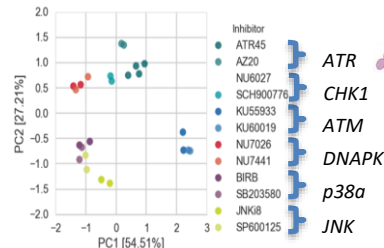
Cell (2019)

Functional mapping of differential signaling by RPTK mutants

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

Alicia Lundby^{1,2,3}, Giulia Franciosa¹, Kristina B. Emdal¹, Jan C. Refsgaard¹, Sebastian P. Gnosa¹, Doris B. Bekker-Jensen¹, Anna Secher¹, Svetlana R. Maurya¹, Indrani Paul¹, Bianca L. Mendez¹, Christian D. Kelstrup¹, Chiara Francavilla¹, Maria Kvelborg¹, Guillermo Montoya¹, Lars J. Jensen¹, and Jesper V. Olsen^{1,2,3,4}
¹Novo Nordisk Foundation Center for Protein Research, University of Copenhagen, Faculty of Health and Medical Sciences, Blegdamesvej 3B, DK-2200 Copenhagen, Denmark
²Department of Biomedical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
³Stem Cell Research and Innovation Center (BRIC), Faculty of Health and Medical Sciences, University of Copenhagen, 2200 Copenhagen, Denmark
⁴Novo Nordisk A/S, Novo Nordisk Park, DK-2760 Maaboe, Denmark
⁵Lead Contact
⁶Correspondence: alicia.lundby@pro.ku.dk (A.L.), jesper.olsen@pro.ku.dk (J.V.O.)
<https://doi.org/10.1016/j.cell.2019.06.028>

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



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Professor, Harvard Med.
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Cancer Institute & Ludwig
Center, Boston

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



Robert Abraham, Ph.D.

EVP, Head Cancer Biology,
Odyssey Therapeutics
Adj. Prof. , Burnham Inst.
Adj. Prof. UCSD

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



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

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

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



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

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

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



Jesper V. Olsen, Ph.D.

Academic Co-Founder

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

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



Jung-Min Lee, M.D.

NCI Collaborator

Investigator, Lasker
Clinical Research
Scholar, NCI

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

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

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

Dosing and Administration

- IV q14d (RP2D = 105 mg/m²)

Safety summary

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

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

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

OVARIAN CANCER TREATMENT LANDSCAPE BECOMING INCREASINGLY CROWDED

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

Exhibit 2 - Notable Ovarian Cancer Presentations at ESMO'24

Company	Drug	Modality	Target	Population	Abstract	Title
IMGN	Mirvetuximab	ADC	FRa	PSOC	718MO	Mirvetuximab soravtansine (MIRV) in recurrent platinum-sensitive ovarian cancer (PSOC) with high folate receptor-alpha (FRa) expression: Results from the PICCOLO trial
GMAB	Rina-S	ADC	FRa	Endometrial/Ovarian	719MO	A phase III study of rinatartab sesutecan (Rina-S) in patients with advanced ovarian or endometrial cancer
STRO	Liveltamab tazevibulin	ADC	FRa	High-grade EOC	749P	Liveltamab tazevibulin, an antifolate receptor alpha (FRa) antibody-drug conjugate (ADC), in combination with bevacizumab (bev) in patients with recurrent high-grade epithelial ovarian cancer (EOC): STRO-002-GM2 phase I study
AZN	AZD5335	ADC	FRa	PRROC	754P	Initial results from a first-in-human study of AZD5335, a folate receptor α (FRa)-targeted antibody-drug conjugate, in patients (pts) with platinum-resistant recurrent ovarian cancer (PRROC)
Coherent Biopharma	CBP-1008	Bi-XDC	FRa/TRPV6	Solid tumors (PROC)	787P	First-in-human, phase I study of CBP-1008, a first-in-class bi-specific ligand drug conjugate (Bi-XDC), in patients with advanced solid tumors
IMGN	Mirvetuximab	ADC	FRa	FRa high OC	746P	Phase III MIRASOL trial: Updated overall survival results of mirvetuximab soravtansine (MIRV) vs. investigator's choice chemotherapy (ICC) in patients (pts) with platinum-resistant ovarian cancer (PROC) and high folate receptor-alpha (FRa) expression
AZN	Datopotamab	ADC	TROP-2	Endometrial/Ovarian	714MO	Datopotamab denuxectan (Dato-DXd) in patients with endometrial (EC) or ovarian cancer (OC): Results from the phase II TROPION-PanTumor3 study
MRK/Kelun	Sacituzumab trimetecan	ADC	TROP-2	Endometrial/Ovarian	715MO	Safety and efficacy of sacituzumab trimetecan (sac-TMT) in patients (pts) with previously treated advanced endometrial carcinoma (EC) and ovarian cancer (OC) from a phase II study
Hengrui	SHR-A1921	ADC	TROP-2	PROC	717MO	SHR-A1921 in platinum-resistant ovarian cancer (PROC): data from a first-in-human (FIH) phase I study
TORL	TORL-1-23	ADC	CLDN6	Ovarian, endometrial, testicular	721MO	Phase I, two-part, multicenter first-in-human (FIH) study of TORL-1-23: A novel claudin 6 (CLDN6) targeting antibody drug conjugate (ADC) in patient with advanced solid tumors
Alphamab Oncology	JSKN003	ADC	HER2 x TOP1	PROC	759P	JSKN003, a HER2-targeting antibody-drug conjugate, in patients with platinum-resistant ovarian cancer: A pooled analysis of two studies
IMCR	Brenetafusp	TCER	PRAME x CD3	PROC	750P	Phase I safety and efficacy of brenetafusp, a PRAME x CD3 ImmTAC T cell engager, in platinum resistant ovarian cancer (PROC)
INCY	INCB123667	Small molecule	CDK2	Advanced Solid tumors (49% OC)	617MO	Safety and tolerability of INCB123667, a selective CDK2 inhibitor, in patients (pts) with advanced solid tumors: A phase I study
ASND	TransCon IL-2 β y	IL-2 pro-drug + chemo	IL-2 β y-R	PROC	762P	First results from phase II dose expansion cohort of transcon IL-2 β y in combination with standard of care chemotherapy for platinum resistant ovarian cancer (PROC) in the IL Believe trial
BNTX/OncoC4	Golistobarb	mAb	CTLA-4	PROC	LBA32	A randomized, phase II, dose optimization of golistobarb, a pH-sensitive anti-CTLA-4, in combination with standard dose pembrolizumab in platinum-resistant recurrent ovarian cancer: Safety, efficacy and dose optimization (PRESERVE-004/GOG-3081)
Hengrui	Fuzuloparib + apatinib	Small molecule combo	PARP/VEGF	Ovarian	766P	A phase II trial of fuzuloparib in combination with apatinib vs. fuzuloparib alone for recurrent ovarian cancer (OC)
Academic	Olaparib + cediranib	Small molecule combo	PARP/VEGF	PSOC	LBA33	ICON9: International phase III randomized study to evaluate the efficacy of maintenance therapy with olaparib and cediranib or olaparib alone in patients with relapsed platinum-sensitive ovarian cancer following a response to platinum-based chemotherapy
Other Notable Long-Term Maintenance Studies						
GSK	Niraparib	Chemo	PARP	Newly-diagnosed advanced OC	LBA29	Final overall survival (OS) in patients (pts) with newly diagnosed advanced ovarian cancer (aOC) treated with niraparib (nr) first-line (1L) maintenance: Results from PRIMA/ENGOT-OV26/GOG-3012
Pharma&GmbH	Rucaparib+ nivo	Chemo+IO	PARP/PD-1	Newly-diagnosed advanced OC	LBA30	ATHENA-COMBO, a phase III, randomized trial comparing rucaparib (RUC) + nivolumab (NIVO) combination therapy vs RUC monotherapy as maintenance treatment in patients (pts) with newly diagnosed ovarian cancer (OC)
Academic	Ganetespib + carboplatin	Small molecule combo	DNA repair inhibition	Ovarian	LBA34	ENGOT-ov48/EUDARIO: European trial on enhanced DNA repair inhibition in ovarian cancer

Source: Jefferies research; ESMO 2024

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

Registrational intent Phase 2b trial

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

¹Subjects with ≥1 on-treatment scan

²<https://ir.acrivos.com/news-events/events-presentations>

Data cut as of 1 April 2024

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

- Endometrial cancer (EC) projected to be the third most prevalent cancer and the fourth leading cause of cancer-related death among women by 2040
 - Incidence = 67,880, prevalence = 865,000 in the US (2023)*; Incidence increasing by 1-3% per year
 - Mortality = 13,250 in the US (2023); 5-year survival ~ 80%*
 - High grade EC accounts for majority of EC deaths each year
- 2L now represents a high unmet need and opportunity for accelerated single agent approval
 - **90% of cases believed to progress to 2L therapy (~27,000 patients in the US/year)**
 - Recent front-line approvals of ICI plus chemo followed by ICI only^{1,2} for high grade EC reduces/eliminates pembro + lenvatinib³ as viable 2L option for most patients
 - **Reported chemotherapy efficacy in 2L is ORR = 14.7% and mPFS = 3.8 months³**
 - Still limited number of early emerging therapies; only Enhertu approved for ~15% of Her2(+++)
- 1L potential opportunity for label expansion in confirmatory trial (maintenance with ACR-368 + anti-PD-1/anti-PD-L1)
 - **New cases of high grade, recurrent EC (progressed on ICI + chemo) ~30K patients/year**
 - Leverage that ACR-368 clinical activity is been seen in patients who progress on prior anti-PD-1 therapy
 - **mPFS in anti-PD-1 maintenance phase ~8.8 months in pMMR (>27 months in dMMR)**

*SEER database

¹Eskander et al, NEJM 2023; ²Mirza et al, NEJM 2023; ³Makker et al, NEJM 2022

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

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

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

*Subject deemed ineligible for anti-PD-I therapy.

[^]1 BM+ and 4 BM- subjects are still on study for follow-up, but no longer receiving study drug.

Data current as of 25 July 2024 and includes all subjects enrolled with registrational intent

BM- includes all subjects treated with ACR-368 + low dose gemcitabine (LDG) at RP2D (105 mg/m² and 10 mg/m², respectively).

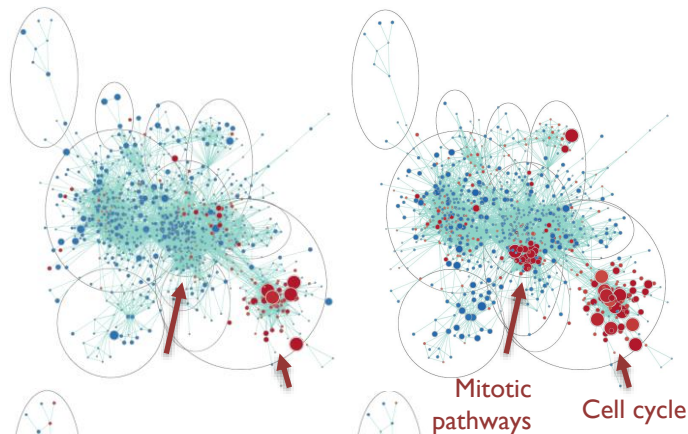
AP3 ANALYSIS: ACR-2316 REGULATES CELL CYCLE AND MITOSIS MORE POTENTLY THAN BENCHMARK WEE1 INHIBITOR

60min
200nM

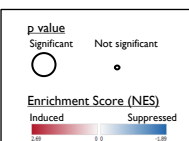
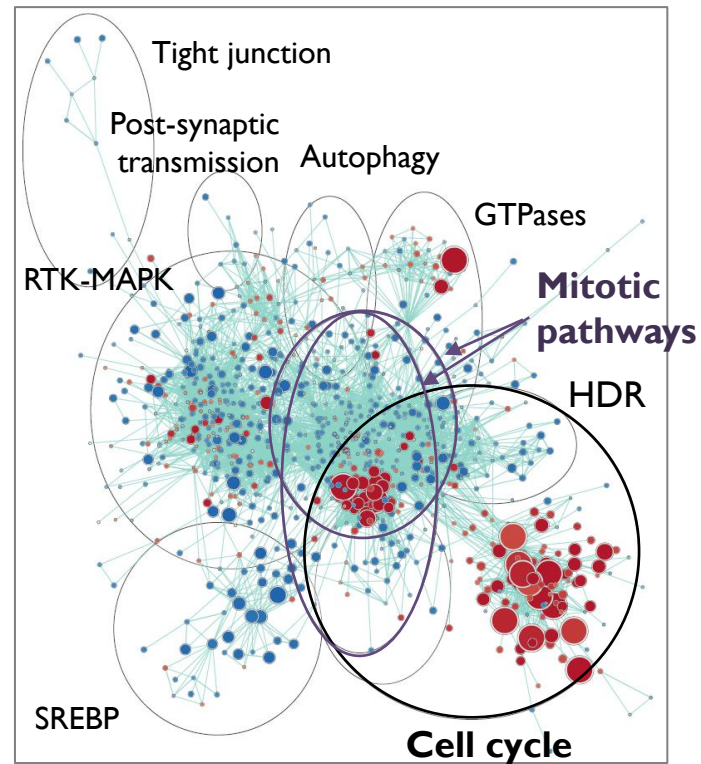
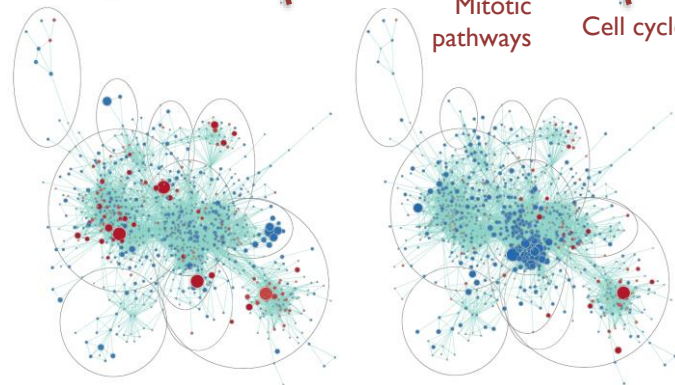
WEE1 inhibitor

ACR-2316

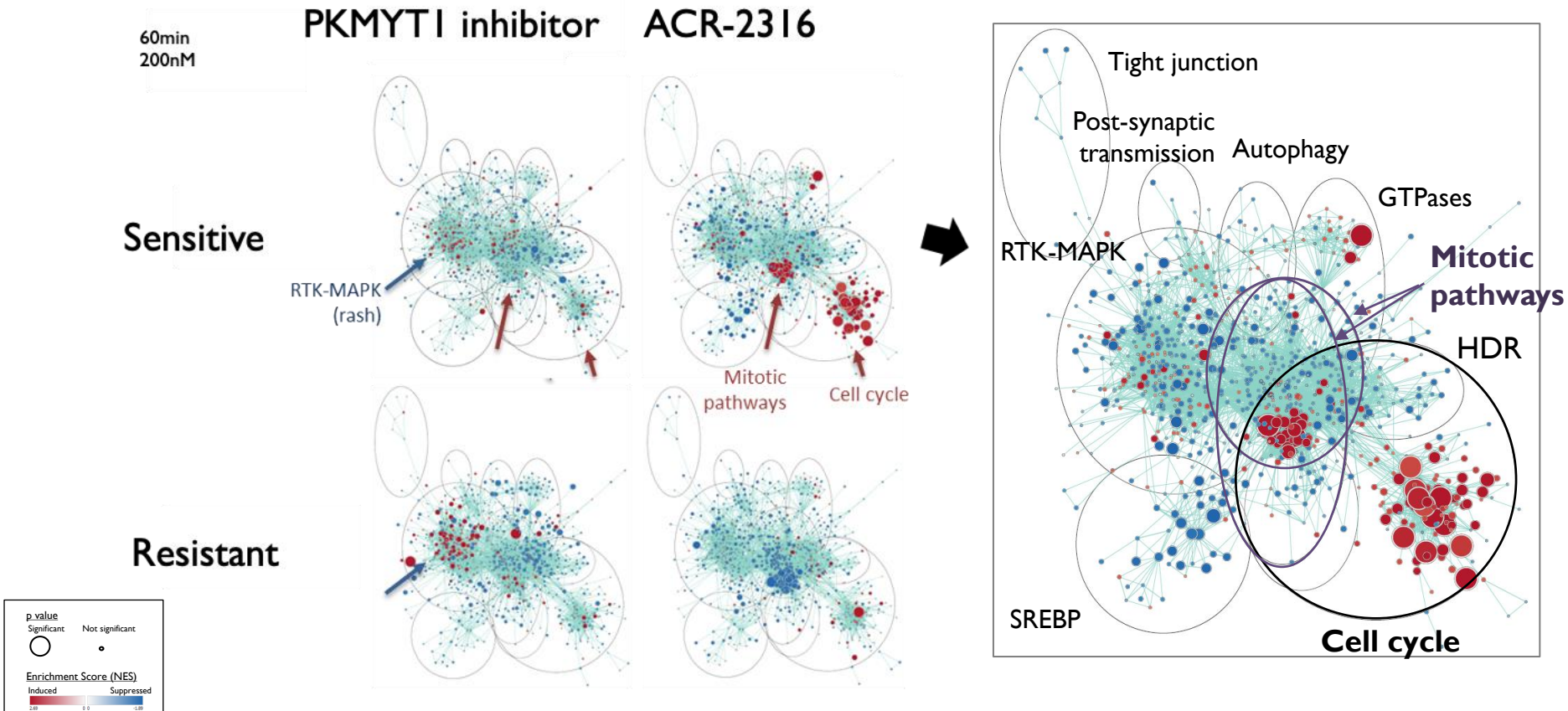
Sensitive



Resistant

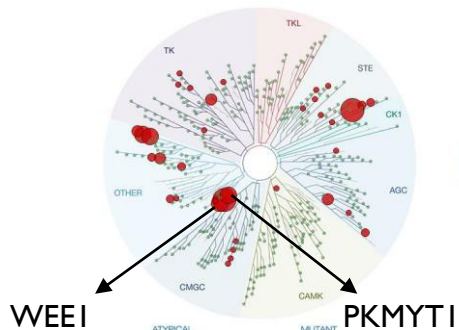


AP3 ANALYSIS: ACR-2316 REGULATES CELL CYCLE AND MITOSIS MORE POTENTLY THAN BENCHMARK PKMYTI INHIBITOR

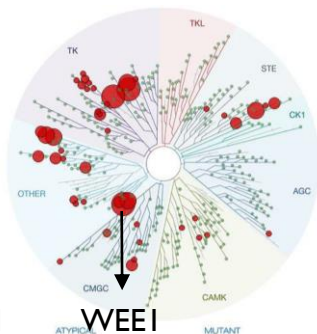


COMPREHENSIVE KINOME SELECTIVITY PROFILING

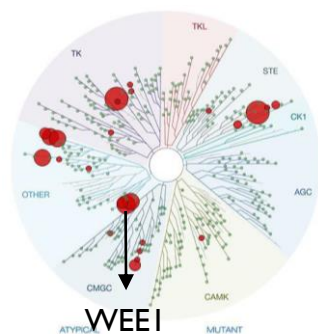
ACR-2316



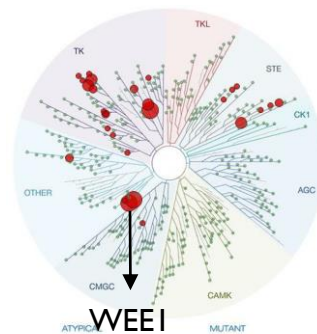
Adavosertib



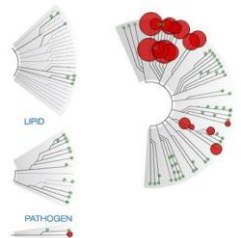
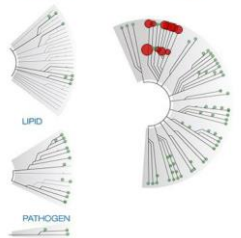
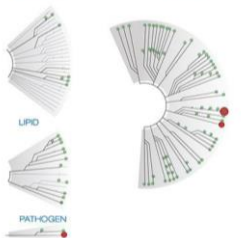
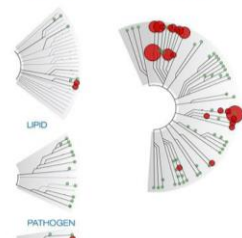
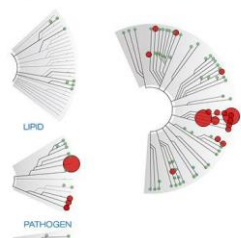
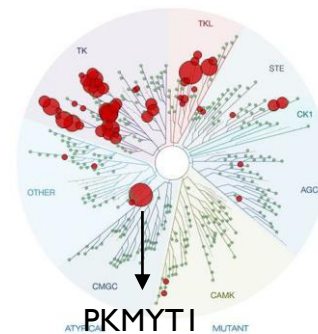
Azenosertib



Debio0123



Lunresertib



468 kinases
@ 1 μ M



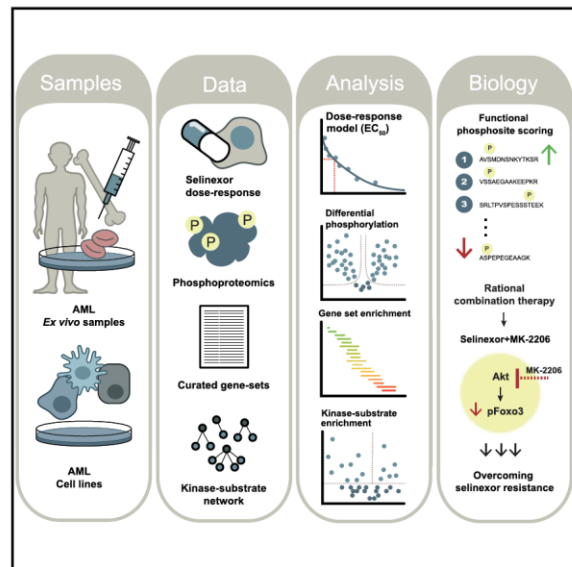
KinomeScan

Cell Reports

Article

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

Graphical abstract



Authors

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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 (RIGHT OF FIRST NEGOTIATION)

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